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FEDERAL OVERSIGHT OF BIOTECHNOLOGY

HEARING

BEFORE THE

SUBCOMMITTEE ON
HAZARDOUS WASTES AND TOXIC SUBSTANCES

OF THE

COMMITTEE ON
ENVIRONMENT AND PUBLIC WORKS
UNITED STATES SENATE

ONE HUNDREDTH CONGRESS

FIRST SESSION

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FEDERAL OVERSIGHT OF BIOTECHNOLOGY

THURSDAY, NOVEMBER 5, 1987

U.S. SENATE,
COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS,
SUBCOMMITTEE ON HAZARDOUS WASTES
AND TOXIC SUBSTANCES,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:03 a.m., in Room SD–406, Dirksen Senate Office Building, Hon. Max Baucus (chairman of the subcommittee) presiding.

Present: Senators Baucus, Lautenberg, Chafee, and Durenberger.

OPENING STATEMENT OF HON. MAX BAUCUS, U.S. SENATOR FROM THE STATE OF MONTANA

Senator BAUCUS. The hearing will come to order.

Biotechnology is a new exciting and profoundly important field of science. It holds great promise for a dazzling array of applications in agriculture, medicine, environmental protection, and manufacturing, just to name a few.

Biotechnology is, in essence, the ability to control and manipulate the basic elements of life, cells, chromozomes, genes, DNA. While the goals of biotechnology are indeed noble, and its accomplishments to date impressive, there is universal agreement that this evolving technology holds many dangers and demands thoughtful stewardship by industry, academia, and by government.

How are we doing so far?

If you ask Dr. Gary Strobel of Montana State University, he would tell you not very well. Last summer, Dr. Strobel injected into 14 elm trees an experimental substance, a biologically engineered organism designed to control Dutch elm disease. He did this without the approval of the Environmental Protection Agency as required under current Federal policy.

What started as an act of civil disobedience soon became a story of national proportions. Not only did Dr. Strobel's act raise a few eyebrows, it raised serious questions about the adequacy of the Federal regulatory structure for biotechnology. Dr. Strobel also raised some fears, fears about a science that is not fully understood by lay-people and, perhaps, I might add by some of its most steadfast supporters.

In this context, those actions may have done some temporary harm. It is vitally important for both the biotechnology industry, in particular, and scientific freedom, in general, that this not become an issue of extremes. Nobody wants an Andromeda strain, the spread of some new organism that could be harmful to people, ani-

mals, to crops, or to the environment, yet we should not choke our biotech industry with excessive or misguided regulations and policies, especially when other nations are aggressively developing their own biotech industries.

After announcing today's hearings, I received a letter from Peter Albershime, Director of the Complex Carbohydrate Research Center of the University of Georgia. His letter sums up the growing concern among the research community. In his letter he states,

> Without taking a position on what Dr. Strobel did and how he did it, it is clear that the morass of complicated and almost indecipherable regulations governing these matters is greatly harming the emerging biotechnology industries of this country.

I agree. I think it is vitally important for this government to permit, indeed, encourage scientific research and development to flourish. Yet, I believe that it is equally important that the scientific and business community understand that the government has responsibility to protect the public safety. These goals are not incompatible. Exploring how we strike the proper balance between safety and aggressive science and biotechnology is one of the goals of this hearing.

The key question to be addressed is one of risk. A recent National Academy of Science paper on the release into the environment of genetically-engineered organisms concluded that a categorical policy must be developed which avoids inhibiting the development and testing of low-risk organisms in the environment, while taking a justifiably cautious approach to high-risk organisms.

It is toward this goal in which I hope to move. I believe we need a single regulatory system for biotechnology development, one that can remedy the problems we are now having, but also one that can cope with this inevitable explosion of knowledge in the future. We need to keep pace with the advance of science.

I also believe that any new system established to regulate biotechnology must be capable of distinguishing between benign creations of the lab and the dangerous ones. This system must not inhibit work on safe substances, rather to facilitate the development of safe biotechnologies into new products and industries.

It must also earn the public's confidence. There must be no doubt that the safety of the public will never be placed at risk and that actions which violate the public's trust not be tolerated. It is my intention to introduce legislation designed to achieve these goals.

It is important that we get our house in order so that both science and industry can move forward. Clearly there is a need for reform and reexamination of how we regulate biotechnology. By learning how the existing regulations operate and how the Strobel incident occurred, Congress will be in a better position to advance both a science of promise and a promise of safety.

In his 1931 address at the California Institute of Technology, Albert Einstein said,

> It is not enough that you should understand about applied science in order that your work may increase man's blessings, concern for man, himself, and his fate must always form the chief interest of all technical endeavors in order that the creations of our minds shall be a blessing and not a curse to mankind.

Einstein's words ring true today, biotechnology is a bold new science and deserves our concern, our encouragement and our respect.

I will now turn to the Chairman of our Committee, Senator Burdick from North Dakota, for his statement?

OPENING STATEMENT OF HON. QUENTIN N. BURDICK, U.S. SENATOR FROM THE STATE OF NORTH DAKOTA

Senator BURDICK. Thank you.

Good morning. I am pleased to be here this morning as the Subcommittee on Hazardous Wastes and Toxic Substances conducts its first oversight hearing during this Congress on the unique problem posed by the release of genetically-engineered organisms into the environment.

I am grateful to Chairman Baucus for his efforts in planning this hearing, and I look forward to working with the Senator and others during this Congress to develop legislation that may be necessary to address the issues raised by the release into the environment of genetically-engineered organisms.

Events of the past 2 years have raised concerns that Federal regulation in this area is not fulfilling two basic requirements.

First, those who use this new technology must know with certainty that regulatory requirements must be met before a genetically-altered organism may be released.

Second, the public must be assured that each potential release is thoroughly studied to assure that no adverse effects to human health and the environment will result if it is allowed to go forward.

Recent events have raised doubt that these fundamental requirements are being met. It is important that researchers be able to predict with certainty that a genetically-engineered organisms released into the environment will not have unintended consequences. It must be assured that no harm will be done to nontarget organisms and that the delicate ecological balance not be upset.

Mr. Chairman, I have other serious concerns regarding the use of this technology. I am deeply concerned about the affect this new technology may have on agriculture, which is so vital to my home State and to us all. I have discussed these additional concerns in a longer statement.

Mr. Chairman, I ask your consent to have the text of my entire statement inserted into the record at this point.

Senator BAUCUS. No objection.

[Senator Burdick's statement follows:]

OPENING STATEMENT OF HON. QUENTIN N. BURDICK, U.S. SENATOR FROM THE STATE OF NORTH DAKOTA

Good morning. I am pleased to be here today as the Subcommittee on Hazardous Wastes and Toxic Substances conducts its first oversight hearing of this Congress on the unique problems posed by the release of genetically engineered organisms into the environment. Events of the past two years have raised concerns that Federal regulation of the release of genetically engineered organisms into the environment may not be serving two vital purposes: providing certainty to industry and academia of the regulatory requirements that must be met in order for any contemplated release to go forward and assuring the public that adverse effects to human health and the environment will not result from such a release. It is becoming apparent that action must be taken by Congress to address these issues. I am grateful to Chairman Baucus for his efforts in planning today's hearing, and I look forward to

working with the Senator and others during this Congress to develop needed legislation.

This Committee's concern focuses on the potential adverse effects of environmental releases of genetically engineered organisms. It is important that researchers be able to predict with certainty that genetically engineered microorganisms released into the environment will not have unintended consequences, such as pathogenicity or toxicity to non-target organisms or an enhanced survival capability that will upset the delicate ecological balance among species of microorganisms. The potential of these altered organisms to spread beyond the site of application and affect the ecology of the surrounding area must also be determined. Another issue of concern, particularly when dealing with microorganisms, is the possibility of transfer of genetic material from one species to another.

The Administration and industry have for years insisted that the existing statutory framework for the regulation of pesticides and toxic substances provide adequate guidance to the Federal regulatory agencies to enable them to meet the challenges posed by the regulation of this new technology. The executive branch is still in the process of writing the regulations, however—a process which has been underway for several years. One problem is that several statutes and agencies are involved. This delay in promulgating final regulations and the labyrinth of agencies and statutes concerned has stymied the efforts of industry to go forward with the technology and has created uncertainty among the public that the potential for adverse effects of releases is being adequately assessed.

In order for mankind to reap the enormous benefits of this new technology and in order for this burgeoning industry to thrive, we must have certainty. Researchers in industry and academia wishing to release a genetically altered organism into the environment must know what permits are required, from which agency or agencies they are to be acquired, and what data need to included in an application for a permit.

The Environment and Public Works Committee's attention will focus on the possibility of relatively immediate adverse ecological effects from these organisms. However, I see in the application of this new technology the potential for other ecological consequences that may not be manifested for some time. Since I come from a State heavily dependent on agriculture, I am deeply concerned over the impact the biotechnology industry will have on farming. The use of traditional breeding techniques has created what some have warned is a dangerous genetic uniformity in major crops such as corn and wheat. I am concerned that the use of the new, highly specific genetic manipulations made possible by this new technology may exacerbate this trend. Genetic engineering has also made possible the virtual "harvesting" of livestock with desirable characteristics. I cannot help but be concerned that the widespread application of biotechnological techniques will create crops and livestock that are replete with desirable characteristics and at the same time incapable of adapting to and surviving an unforeseen environmental stress. Evolution would have been impossible without an abundant, diverse supply of germplasm. Surely we are not so confident of our technological prowess that we think it advisable to predetermine the precise genetic makeup of the crops and livestock on which our lives depend and completely forgo the inherent safety of the diversity of characteristics nature has provided.

I am also concerned about the economic and social consequences the widespread use of this new technology may engender. For a generation now we have seen the decline of small, family-owned farm and the advent of enterprises of enormous acreage, heavily dependent on chemicals and sophisticated machinery. Farmers find it impossible to compete in the marketplace without resorting to the modern cultivating techniques their competitors use. These entail a great reliance on outside interests to supply items such as hybrid seed and commercial fertilizers and pesticides. Someday we may have patented seeds that have been genetically engineered to increase their herbicide resistance that will be sold in conjunction with a patented, compatible herbicide. The patent for both the seed and herbicide might belong to the same company or individual. This may not be an undersirable situation, but I think it would be most prudent before we go forward with this technology to assess what potential it may have for effecting an increased concentration of wealth and economic power. In this case, it isn't only money.

I believe that because there are fewer farms and farming methods are becoming increasingly homogeneous, there is an increased possibility that a single mistake or combination of mistakes in judgment may result in catastrophe. Therefore, before we adopt this new technology we must be certain what its environmental consequences will be.

I also want to mention that I believe that there are serious ethical questions raised by the manipulation of the genetic material of animals, particularly when such manipulation involves the transfer of genetic material from one species to another.

I have heard much about the promise of this new technology. Biotechnology is being touted as our salvation from problems such as overdependence on pesticides, the lack of adequate toxic waste disposal, methods, the energy shortage, and famine. But it is important that we not rush into the use of this new technology without a thorough assessment of its ecological implications. We must not forget, in our zeal to go forward with this promising technology, that lack of foresight was one of the primary causes of these problems.

Senator BAUCUS. I would like to call our first panel to the table.

Dr. Luther Val Giddings, Biological Applications Program of the OTA; Dr. John Moore, Office of Pesticides and Toxic Substances, EPA; Dr. William Gartland, Office of Recombinant DNA Activities at the NIH; and Dr. Kenneth Gilles, Office for Marketing and Inspection Services at the USDA. Gentlemen, why don't you begin.

First, Dr. Giddings, why don't you proceed.

Senator BURDICK. Mr. Chairman, I would like first to welcome to this committee an old friend of mine from Fargo, North Dakota. We have flown him down here to Washington to get things fixed up. I am talking about Mr. Gilles.

Welcome to the committee.

Dr. GILLES. Thank you, sir.

STATEMENT OF DR. LUTHER VAL GIDDINGS, BIOLOGICAL APPLICATIONS PROGRAM, OFFICE OF TECHNOLOGY ASSESSMENT, WASHINGTON, DC

Dr. GIDDINGS. Good morning. My name is Val Giddings. I am pleased to be here and honored to have been asked to testify.

For more than a year now I have been directing an OTA study to examine scientific issues relevant to the planned introduction of genetically-engineered organisms into the environment. Our report is in the final stages of preparation. Since it has not yet been delivered to the Technology Assessment Board, however, I am not yet free to discuss in any great detail the findings or the issues and options for congressional action that form part of study.

There is abundant information available in the public record, however, and it is primariiy upon this information that I will base my comments this morning.

It is no longer news that recombinant DNA and other new biological techniques have brought new vitality to many industries. Researchers can now do much more rapidly many things that used to be prohibitively expensive in time and labor. They can screen large populations of plants or animals for desired genetic characteristics without waiting for mature adults to develop. They can move genetic material quickly and relatively easily between species where it would previously have been difficult or impossible.

They can also now do some things that were simply not possible before. They can insert specific structural genes or control sequences precisely where they want to, without accompanying genetic material that might complicate the interpretation of results. They can induce precise, site-specific mutations to study the effects of particular changes in gene structure on patterns of gene regulation and the development of organisms.

The power that these new capabilities brings for good, the power to improve our quality of life, has been widely publicized and sometImes oversold. Some people are understandably concerned, however, about the potential for problems that might be associated with these new techniques. Although some disagree, I think these people ask legitimate questions, questions that need to be asked.

As part of our study of this issue, we decided that it would be valuable to have precise data on the public opinion about biotechnology and, particularly, about deliberate releases of engineered organisms. We, therefore, commissioned a public opinion survey by Louis Harris and Associates.

This survey has now been published and it forms Publication Number Two in our series of studies of new developments in biotechnology. If you have no objection, I would make that a part of my written comments to submit. (See p. 60.)

Senator BAUCUS. Without objection.

Dr. GIDDINGS. I will briefly highlight four of the results of our survey.

We found that when faced with the fundamental choice between the risks and benefits to society from continued technological and scientific innovation, a majority of the public, 62 percent, says that it feels that the benefits outweigh the risks. In contrast, 28 percent of the public says that it feels that the risks outweigh the benefits.

A large majority of the public, 82 percent, says it favors environmental applications of genetically-altered organisms on a small-scale experimental basis. In fact, 53 percent say they would favor this and 14 percent state they would not care if their own community were selected as a site to test a genetically-altered organism.

However, at the time the question was asked, only 42 percent of the public said it thought commercial firms should be permitted to apply genetically-altered organisms on a large-scale basis, which of course is the ultimate objective of doing field tests, assuming they go well.

In addition to supporting research, the public also sees another important role for government in the development of biotechnology, that is, regulating and assessing potential risks. When asked "who should be responsible for deciding whether commercial firms should be permitted to apply genetically-altered organisms on a large-scale basis?," a plurality said they felt that a government agency should decide.

However, the survey also identifies a potential credibility problem in governmental involvement in biotechnology. The public believes that Federal agencies are distinctly less able than university scientists to assess potential risks. Moreover, in disputes between Federal agencies and environmental groups over risk statements, the majority of the public says it is inclined to believe the environmental groups.

Finally, while the public expects strict regulation to avoid unnecessary risks, obstruction of technological development is not a popular cause in the United States in the mid-1980s. Our survey indicates that a majority of the public says it believes the expected benefits of science, biotechnology, and genetic engineering are sufficient to outweigh the risks.

In conducting our assessment of this topic, we have found that there is much that scientists know and understand that is relevant to planned introductions, and much useful experience that can provide guideposts as to how to proceed. But there are also many important uncertainties. Some of these can be addressed by basic research, others only by carefully designed and monitored field tests.

There are a number of questions that one might ask to shed light on these topics. The most important class of questions includes those that I think ought to be asked, questions that by being asked clarify the useful perspective, the illuminating perspective, the point of view that might help a regulator deal with the issue in a practical manner.

Such illuminating questions include the following: How does recombinant DNA or other of the new techniques of modern biotechnology differ from methods that have been used for decades, centuries or millennia?

What can be accomplished with these new techniques that would not have been possible with the older techniques?

Are there unique benefits or problems associated with these new techniques?

If there are unique benefits, is is not logical to expect that there might be unique problems?

If there are, what might they look like?

Is there a demonstrable need for regulation specific to the new techniques?

Perhaps most importantly, what are the relative costs and benefits of the new techniques as opposed to the older, established, or classical technologies, many of which are now regulated less than are products produced with these new methods? What costs might be associated with excessive regulation?

Addressing questions such as these can do a great deal to placate public concern and smooth regulatory paths for the products of biotechnology.

In closing, although I am limited in what I can discuss from our assessment of these issues, I would like to describe, in broad terms, some of our primary conclusions.

Our assessment has found that, while there are reasons to be cautious, there is no cause for alarm at the prospect of planned introductions of genetically-engineered organisms into the environment. While support for relevant research, both fundamental and applied, will reduce some important uncertainties, some questions can be answered only with practical experience. Realistic small-scale field tests are likely to be the only way in which some uncertainties about planned introductions can be resolved.

Two final points: genetically-modified organisms will contribute substantially to improved health care, agricultural efficiency, and the amelioration of many pressing environmental problems that have resulted from the extensive reliance on chemicals in both agriculture and industry; and the scientific community urgently needs to provide guidance, both to investigators and regulators, in evaluating planned introductions of modified organisms from an ecological perspective.

Those last two points I mentioned, of course, were taken verbatim from the recent National Academy of Science's position paper on this question.

I thank you for this opportunity to testify and I would be happy to respond to any questions you might have.

Senator BAUCUS. Thank you very much, Dr. Giddings.

Our next witness is Dr. John Moore with the Environmental Protection Agency.

Welcome, Dr. Moore.

STATEMENT OF DR. JOHN A. MOORE, ASSISTANT ADMINISTRATOR, PESTICIDES AND TOXIC SUBSTANCES, U.S. ENVIRONMENTAL PROTECTION AGENCY

Dr. MOORE. Senator, I apologize for being late.

Senator BAUCUS. No problem. Senators are always on time, as you know.

Dr. MOORE. Senator, I ask that my statement and three appendices be inserted into the record, and I will just highlight points that are in that testimony, with your permission.

Basically, EPA as relates to biotechnology asserts that it can regulate and should regulate, using two of its statutes. That is the Toxic Substances Control Act and the Federal Insecticide, Fungicide, and Rodenticide Act.

In the policy that we promulgated along with our sister agencies in June of last year, we articulated three categories of microbes—no matter what their ancestry may be, natural or engineered—that are of particular concern to EPA. Along with the microorganisms used in the environment and therefore having the potential for widespread exposure; micro-organisms with new characteristics or characteristics that would be new in the environment in which they were proposed to be placed; and then pathogens or organisms containing genetic material from such pathogens, because of the demonstrated ability to cause adverse effects.

In looking at the development of an organism, in this case for constant commercial ventures, we see three distinct phases being involved. One is the early small-scale field testing, followed up, if successes are met with the small-scale, probably with larger scale testing and then ultimately leading to commercialization of a product. In some instances, wide-scale commercialization may well coalesce into a single step.

We identified that under TSCA that one would have to implement some rules in order to have the full breadth of TSCA be brought to bear on this issue. We talk about amending Section 5 exemptions from the research and development perspective so that, indeed, non-indigenous organisms and new organisms would not be automatically exempt even at the small-scale field testing stage. Also, to have another mechanism in place that basically would capture the organisms that were pathogen derived of one sort or another.

We have moved forward with a review process that has focused on the small-scale field testing, because that is basically the crux of where everybody is in the development of products as we sit here today. We have adopted a process that is similar, whether it is the

FIFRA Statute or TSCA Statute that is being utilized, basically, will review material, upon receipt in the Agency, from the standpoint of completeness on the scientific issue that might be associated with the proposed testing.

We then will draw comments from within the Agency on that analysis and that proposal for experiment and, as appropriate, we will draw on comments from agencies elsewhere in the Federal government, most commonly the USDA. We also will alert State regulatory agencies to alert them to the submission and the possibility that something might be proposed to be done within their state.

If appropriate, we also have aggressively used an independent peer review process, drawing upon scientific expertise in that area that may be found within the academic community. Even if we elect not to use an independent peer review process in a formal sense, we almost always will consult with the chair of that panel to see if he or she concurs with our judgment as to the need for a more formal review.

To date, the Agency's assessments have been endorsed by peer review processes. We have conducted 16 reviews under the Pesticide Statute, five reviews under the Toxic Statute, and these are described in detail in the appendix to my testimony. The results of that is that there has been approval given by EPA to field test recombinant DNA organisms in three instances; two in California, one in South Carolina, and it is anticipated that next year another one will be conducted in Wisconsin.

Thank you.

Senator BAUCUS. Thank you, Dr. Moore.

Dr. Gartland.

STATEMENT OF DR. WILLIAM GARTLAND, OFFICE OF RECOMBINANT DNA ACTIVITIES, NATIONAL INSTITUTES OF HEALTH, BETHESDA, MD

Dr. GARTLAND. Thank you, Senator.

I would like to summarize my statement. I would like to discuss the role of the NIH Recombinant DNA Advisory Committee and the NIH Guidelines for Research Involving Recombinant DNA Molecules in the oversight of recombinant DNA research.

The NIH was the first Federal agency to exercise oversight of experiments involving recombinant DNA. The NIH established the Recombinant DNA Advisory Committee, or RAC, in response to a request from the National Academy of Sciences.

The original NIH guidelines were issued in June of 1976. These guidelines specify safeguards to be utilized in the course of experiments. The guidelines also specify certain administrative requirements under the Roles and Responsibilities section. Approximately two and one-half years passed between the issuance of the original NIH guidelines in June of 1976 and their first major revision in December of 1978.

The guidelines as revised in December of 1978 incorporated a number of new features. Among them, five classes of experiments agreed to pose no novel hazards were exempted from the requirements of the guidelines for laboratory research. There was also a

general reduction in the level of containment in most experiments covered by the guidelines.

The revised guidelines also broadened representation on local Institutional Biosafety Committees, requiring that individuals not affiliated with the institution be included in the membership. At the time of the 1978 revision, the membership of the NIH Recombinant DNA Advisory Committee was increased and broadened—before the revision, the RAC was composed of 14 members, of which two were non-scientists. The current RAC consists of 25 voting members, including scientists and non-scientists, and also there are representatives of 15 relevant Federal agencies that have non-voting membership on the RAC.

The revised guidelines specified three classes of actions, and under the so-called "major" actions, a mechanism was incorporated for the future evolution of the guidelines. Using this mechanism, modifications have been made in the guidelines at virtually every RAC meeting since December of 1978.

Under the revisions of the guidelines issued in April and August of 1982, Section III of the guidelines which specifies containment conditions for covered experiments was reorganized and greatly simplified. All experiments now fall into one of four classes. Certain experiments continue to require prior review by the NIH; certain experiments continue to require review by an institutional biosafety committee; certain experiments require notice to an institutional biosafety committee simultaneously with initiation of the experiment; and certain experiments continue to be exempt.

I would now like to summarize the evolution of the guidelines with regard to release into the environment of organisms containing recombinant DNA molecules. The original version of the guidelines, issued in 1976, specified that five classes of experiments were not to be initiated at the present time. Among these were experiments involving the deliberate release into the environment of any organism containing recombinant DNA molecule.

In the first revision of the guidelines in December of 1978 this prohibition was retained. However, the 1978 guidelines permitted exceptions to prohibited experiments provided that the experiments were approved by the NIH Director following publication in the Federal Register for comment and review by the Recombinant DNA Advisory Committee.

In the April 1982 revision of the guidelines experiments that were previously prohibited were placed in a new section of the guidelines entitled "experiments that require RAC review and NIH and IBC approval before initiation." Included again in this category was release into the environment. The procedures for approval remained the same, but the use of the term "prohibited" was dropped at that point.

The revision of the guidelines issued in June of 1983 incorporated new procedures for approval of field testing under certain specified conditions of certain plants modified by recombinant DNA techniques. Plants that meet these requirements now required review by the RAC Plant Working Group, but no longer by the full RAC, prior to an NIH approval.

In November of 1985 a new provision was added to the section of the guidelines that pertains to experiments that require RAC

review and NIH and IBC approval before initiation. That provision stated that

> If the experiments in this category are submitted for review to another Federal agency, the submitter shall notify the NIH Office of Recombinant DNA Activities. The Office may then determine that such review serves the same purpose and, based on that determination, notify the submitter that no RAC review will take place, no NIH approval is necessary, and the experiment may proceed upon approval from the other Federal agency.

In August of 1987, this provision was revised and broadened to cover all recombinant DNA experiments, and it currently reads "Any recombinant DNA experiment which according to these guidelines requires approval by the National Institutes of Health, may be sent by the submitter to the NIH or to another Federal agency that has jurisdiction for review and approval. Once approval or other applicable clearance, has been obtained from a Federal agency other than the NIH (whether the experiment is referred to that agency by the NIH, or sent directly there by the submitter), the experiment may proceed without the necessity for NIH review and approval." Then, there is a restriction dealing with human gene therapy that says those experiments still require NIH review.

The NIH anticipates that most experiments involving release into the environment of organisms containing recombinant DNA will fall under the jurisdiction of other Federal agencies.

Thank you.

Senator BAUCUS. Thank you Dr. Gartland.

Our final witness is Dr. Gilles.

Would you proceed, Dr. Gilles?

STATEMENT OF DR. KENNETH GILLES, ASSISTANT SECRETARY MARKETING AND INSPECTION SERVICES, U.S. DEPARTMENT OF AGRICULTURE, WASHINGTON, DC

Dr. GILLES. Mr. Chairman, it is my pleasure to be here to discuss the Department of Agriculture's regulation of biotechnology. Accompanying me here today is Terry Medley, who might become involved with more of the technical details.

I would like to paraphrase our statement and include that in the record and, in addition, an appendix which I would like to add at this time.

It is vital that the products of biotechnology be regulated based on firm scientific principles, and the same high standards of safety and efficacy as are those products made through conventional technology. We seek to foster a regulatory climate in agriculture that encourages innovation, development and commercialization of beneficial new agricultural products derived from biotechnology, while at the same time implementing a responsible policy that limits potential or real risks.

The USDA regulatory policy is focused on three main points. The first is that existing statutes are adequate to regulate the products of agricultural biotechnology. The second is that biotechnology products would not differ fundamentally from those products produced by conventional methods, and this is one of the conclusions of a recent National Academy of Science study. Three, that the product and the risk should be regulated rather than the technology.

The USDA carries out its regulatory responsibility under a variety of authorities. Statutes administered by the USDA and applicable to the regulation of biotechnology have been listed in the USDA policy statements published in the Federal register. I will not go into those at this time, but because APHIS has been the most actively involved agency, to date, in regulating and testing the development of genetically-engineered organisms, I would like to focus a few comments on APHIS's activities and efforts.

Veterinary biological products are regulated under the Virus-Serum-Toxin Act, which dates back to 1913. Amendments to the this Act were contained in the Food Security Act of 1985 and they expanded APHIS's authority over certain veterinary biological products. APHIS published final regulations implementing the 1985 amendments during the spring and summer of this year. These regulations are in place. All requirements are designed to ensure that the product is pure, safe, potent and efficacious.

The veterinary biological products produced by recombinant methods are evaluated on a case-by-case basis using the same stringent standards for licensing employed for conventionally produced biologics. To date, APHIS has issued some 21 product licenses for products manufactured from the biotechnology processes.

The APHIS safety review process involving products containing recombinant-derived modified live organisms include an environmental assessment of all field tests and licensing actions. The availability of these environmental assessments is announced to the public by publication in the Federal Register.

In another area, the Federal Plant Pest Act and the plant Quarantine Act are the basis for the new rules recently published for genetically-engineered organisms, which may or could be considered plant pests.

The final rule, which took effect on July 16, established a permit and other requirements for the importation, the interstate movement, and the release into the environment of genetically-engineered organisms and products that are or may be considered plant pests. These products are regulated for their potential risk, if the product consists or contains an organism listed as a plant pest. The rule requires that we notify the States so that they may review permit applications also. Although the rule was published as final rule, it is flexible enough to be amended whenever necessary to reflect the changes in technology.

Since the final rule took effect, APHIS has received 24 applications for movement and six applications for environmental release of plant organisms. For each application for release, APHIS prepares an environmental assessment according to the requirements of the National Environmental Policy Act. Anyone who violates our regulations on plant pest, veterinary biologics, or animal pathogens is subject to a range of administrative, civil and criminal penalties.

We are confident that we are meeting our responsibilities in a way that will make the products of biotechnology available to our agricultural community as quickly as possible, while ensuring that full protection is provided for agriculture and the environment.

Thank you very much, Mr. Chairman.

Senator BAUCUS. Thank you, Dr. Gilles.

I note the presence of Senator Chafee, he is constantly playing an active role on environmental issues.

I wondered, Senator, if you have a statement you would like to make at this point?

Senator CHAFEE. Thank you, Mr. Chairman.

Unfortunately, I had to be over in the House testifying on a Radon Bill, which you have been active in also, and thus was not able to be here.

I am interested in this area. It seems that there is one thing about this committee: we don't solve all problems, but new problems keep coming along. It is an active committee and we appreciate your leadership on this subcommittee.

Senator BAUCUS. Senator Lautenberg was here earlier. He is going to try to return later, time permitting.

Gentlemen, a key question, I think, in the minds of all of us is whether the present statutes are adequate and are sufficiently keeping up with the development of science.

It is obvious that genetic-engineering is moving us as a society more and more away from random selection of biological development, and more into planned, engineered biological evolution development. It is fraught with all kinds of dangers, because it speeds up the process much more quickly than if the process were random.

I would like each of you to say, candidly, the degree to which you think your agency and, particularly, the statutes which you administer are keeping up.

I might note that most biological engineering has developed rather recently, over the last 15 years, and these statutes have been here longer than 15 years.

In your answer I would like you to address the degree to which genetically-altered material regulation is different from or the same as the chemical regulation. For example, TSCA and particularly FIFRA. FIFRA regulates pesticides and TSCA is hazardous substances, which are chemical. They are basically inorganic substances.

I am wondering if you could just tell me the degree to which you think those statutes are adequately or are not adequately regulating biologically-engineered development, which is a new phenomenon and basically not contemplated when these statutes were written?

We will start with you, Dr. Moore.

Dr. MOORE. Mr. Chairman, the FIFRA statute is a very old statute as you well know. However, in judging its effectiveness, its utility, as you get into genetic engineering of one sort or another, surprisingly to some, the nature of the statute and regulations that have been promulgated under that statute, I think, lend very nicely into the issues that face biotechnology. So I am very comfortable with it.

Senator BAUCUS. Essentially, why?

Dr. MOORE. FIFRA is a licensing statute, to begin with, in addition to that it has developed over the years a perception that indeed one also has to keep track of the development of a chemical and a microorganism, even prior to the stage of being granted that

commercial license. It has this practice in place that has stood very well over the years in the experimental use permit.

One change that I think we promulgated in 1984 was a change of policy. In the past we had had an exemption that if you were proposing to do a field study that involved less than 10 acres of land or one acre of water that you did not need an experimental use permit. For non-indigenous organisms of any sort, we modified that policy back in 1984 and we affirmed that modification.

Senator BAUCUS. I asked that question because some suggest and, in fact, it is true that biological substances can grow and multiply in some environments. They may be dormant in other environments, but should the environment change after they are in the atmosphere or in the ground or wherever, they could then multiply and grow, whereas, most other chemicals don't have those properties.

Does that difference mean that the statutes should be modified, or is that difference meaningless as far as you are concerned. Some would suggest that that is a very real difference and, therefore, we have to change and modify to address that difference?

Dr. MOORE. Senator, there is certainly a real difference between micro-organisms and chemicals, but we have been successfully regulating microorganism and pesticides before the advent of recombinant DNA. I just think the statute lends itself to it.

Senator BAUCUS. But, isn't it true that EPA has interpreted TSCA to include, even though there is no language that says so?

Dr. MOORE. The Agency asserts that TSCA does have jurisdiction in this area. There have been other people who have publicly stated that they question what the force is. While we are comfortable in asserting that it does, nobody has yet gone to court to get the court to rule whether or not the Agency's assertion is correct or incorrect. We continue to move forward under the assumption that TSCA does apply.

I think what we have to do in TSCA, however, is that, I believe, we have to get into a rulemaking that allows us to have better holds, as appropriate, a hold at some of the early developmental stages of products.

There is a research and development exemption embodied in the TSCA statute. We don't think that exemption necessarily is appropriate for non-indigenous organisms, including those that are engineered. We would like to change that, I think, in rulemaking and have it mimic more closely the approach that is under the Pesticides Act.

Senator BAUCUS. Dr. Gilles, I wonder if you could address the question of whether the different nature of biologically engineered organisms is different enough to require some changes in the statutes or not?

Dr. GILLES. From the standpoint of Agriculture, Mr. Chairman, we feel that there are sufficient statutes on record to accommodate our needs at the present time. I think one must put into perspective the fact that agriculture really is applied biology, if you are growing plants; zoology if you are growing animals. As a consequence, we have been dealing with genetics for many years. As Chairman Burdick is fully aware, this has been the area in which I have been operating for about three decades.

I recall some years ago, when we began working on weeds, there was an area where our scientists indicated they needed to plant some weeds, and this was a horrible experience to those people who felt that they were doing work on applied genetics—why study weeds?—but, indeed, by knowing the life cycle of the plant pests as well as the life cycle of those organisms that are desirable, from the standpoint of agriculture, it not only improves your knowledge base but improves your ability to control the desirable attributes or the undesirable attributes.

Again, from the standpoint of agriculture, I think, we feel that the statutes are adequate and, to a degree, we are quite familiar with the background. We consider biotechnology to be, really, an extension of much of the genetic work that has been going on for a long period of time.

Senator BAUCUS. I have many more questions, but I see my time has expired.

Senator Burdick.

Senator BURDICK. Dr. Gilles, you more or less answered what I had in mind.

Are the statutes and the regulations adequate to do a good job in this new field of genetic engineering right now? Do we need anything more?

Dr. GILLES. At this time, I think they are adequate. They may require fine tuning as we learn more about the system. As we learn more about the potential for both regulation and opportunities for production in the future, I believe we have the statutory authority in place. Ultimately, to do a better job, we may need to change and modify rules and regulations.

Senator BURDICK. My question came from the area of agriculture. That is what you are speaking to?

Dr. GILLES. Yes, sir. I was speaking from the agricultural standpoint.

Senator BURDICK. Thank you.

Senator BAUCUS. Senator Chafee.

Senator CHAFEE. Thank you, Mr. Chairman.

I would like to refer you folks to page nine of Dr. Strobel's testimony, who is going to be testifying next.

He says,

To me it appears that the proliferation of regulations is putting unreasonable restraints on people who are honestly trying to solve major problems facing our society. Some of the scientific and technological problems that our nation faces are extremely difficult to handle.

On top of this, we have imposed a sea of regulatory actions by a myriad of Federal agencies with conflicting definitions. The entire effect is one that is absolutely impossible for a scientific researcher (especially in a small business or academic institution).

I am not sure whether the "small" reflects on the "academic institution," modifies academic institution or not, or whether all academic institutions are put under this handicap.

. . . to comprehend and to follow on a regular basis. At the same time, there is need for a system to assure the public of the safe application of a new and largely misunderstood scientific discipline. As a voice from the wilderness of America, and as one who has suffered the consequences of this complex system, I feel that the time has come for sweeping changes in how we think about biotechnology and how we regulate it.

What do you say to that, Dr. Gartland?

[Pause.]

Senator CHAFEE. Right.

In law school, we used to have a technique, when they would ask a general question, if you kept your eyes down you were fairly safe of not being fingered; if you looked up it was a sense of eagerness, similar to raising your hand.

I saw your name plate first, and I thought——

Dr. GARTLAND. Senator, I can only respond really from the viewpoint of the NIH guidelines. As I mentioned in my statement, in the 1982 revision of the guidelines, we simplified the whole structure so that experiments now fall in four classes based upon the review mechanism: whether you have to come into the NIH, or whether you have to have prior approval by the IBC, or just notify your IBC, or whether you are exempt. We did that to try to simplify things for investigators and biosafety committees.

After that revision was issued, a couple of years ago, we did a survey of all the IBCs. We sent out a questionnaire and asked them if they were having any serious problems with this scheme that we had instituted The answers that came back, essentially unanimously, indicated that there were no serious problems with it.

Senator CHAFEE. You think Dr. Strobel is just off base. I must say, I read over his testimony and, first of all, I think it is splendid that somebody is trying to do something about the Dutch elm disease, because obviously it has effected the area of the country that I come from rather badly, but at the same time I noticed, through a variety of factors, he thought he was doing the right thing, but I must say he notified, I think, EPA on June 15th, and started his experiment on June 18th, which doesn't seem to give anybody much leeway, but he says that there is no way to work your way through this maze.

Goal 1) we need to develop a single document—a "constitution of biotechnology" that is readily available to all practitioners, institutions, biosafety committees and companies doing biotechnological activities in the United States. Such a document should be easy to read, rational, and workable.

Do you think he has a case?

Dr. GARTLAND. My comments were basically directed towards the NIH guidelines. The Federal government did make an attempt in the coordinated framework, which was issued in June of 1986, to, in fact, do that, to have a single document that would have the major policy statements of NIH, FDA, EPA, USDA and, I think, OSHA is in there. I imagine there are a number of implementing regulations that are apart from that document and I don't know the full details.

Senator CHAFEE. I am not asking you about Dr. Strobel's specific case, obviously, but he is down there in the hustlings, to mix a metaphor, he is on the front lines, and trying to do something about this and should somebody in his position, not taking him specifically, but do you think somebody in his position has, at the present time, available to him sufficient guidelines to stay on the straight and narrow path?

Dr. GARTLAND. I think the guidelines are out there. I think they are sufficient. They are complex, Senator. I will admit that. I think people have been living with the NIH structure for over ten years.

They are comfortable with it. They know what they have to do. We now have a lot more complex structure within the last year or two that, I think, will take some getting used to.

Senator CHAFEE. This whole area is so complex. I don't know what is NIH, and what is the Department of Agriculture's area. You are presumably in medical research. I mean medical researchers would heed your guidelines, whereas, if you are doing agricultural work, you would be paying attention to what Dr. Gilles has propounded. Is that correct, Doctor?

Dr. GILLES. In general that is correct, Senator.

Senator CHAFEE. The word 'in general' encompasses many sins.

Dr. GILLES. Primarily, the NIH leadership should be recognized and, as Dr. Gartland has indicated, the guidelines have been in place for NIH since 1976, so they provided the leadership under a broad umbrella. I believe any research that was conducted under Federal financial sponsorship should follow the research guidelines.

Senator CHAFEE. This is what the EDF, the Environmental Defense Fund, Ms. Goldburg, is going to testify to shortly after you.

The USDA is an inappropriate lead agency to regulate releases of engineered organisms for two reasons. First, USDA's mandate is to protect and enhance agriculture and forestry in the United States. Like all agencies, it is bound by NPA and must disclose the environmental implications of its decisions, but USDA has no mandate to protect the environment. Even if they did, it has no legal basis for strong regulation.

Second, USDA is in the strange position of promoting the development of agricultural biotechnology while also regulating its products. As experienced, the Atomic Energy Commission painfully demonstrated such divergent goals can only breed internal conflict.

What do you say to that one?

In other words, what she is saying is that you are out to promote the development of biotechnology and then you are regulating on the other hand, and that is a conflict that shouldn't exist.

Has she got a case?

Dr. GILLES. I would take severe exception to some of these statements. I have not had a chance to read her entire statement, so I can only react to that which you have commented on.

I think it may show a lack of appreciation of the fact that for many decades the Department of Agriculture, indeed, has promoted, worked to improve the plants and animals which constitute our food supply. In the broad sense, these primarily were, in terms of the current context, biotechnology-devised organisms.

When you go through a plant breeding program, you make selections, you make crosses, you might make modifications, and one view of biotechnology, as it is now being developed, is simply that you can make these modifications under more controlled procedures, and you can make them more rapidly.

Senator CHAFEE. My time is up, why don't we hold off there. My time has gone by and I don't want to cut you off totally.

Dr. GILLES. Senator, can I make just one comment?

Senator CHAFEE. Sure.

Dr. GILLES. I think over the years, sticking just with the plants for a minute, we have worked very diligently, one, to increase plant productivity, and at the same time, we have worked to note that increased plant productivity means very frequently that you

have control of the microorganisms and the pests that act on those plants.

Wheat rust, for example, is I think a good example. If we were to release wheats that were susceptible to rust, the ultimate yield would go down. That would depress productivity, so we have learned how to control wheat rust.

Senator BAUCUS. Dr. Gilles, pulling up on that, it sounds to me like one could make the argument that still the USDA is the fox guarding the chicken coop. You have two simultaneous goals here.

Senator CHAFEE. The goals that I cited?

Senator BAUCUS. Exactly.

Senator CHAFEE. Out to develop and at the same time to regulate.

Dr. GILLES. I guess I don't share your thoughts on this, Senator. Just as HHS has a research responsibility in NIH and a regulatory responsibility in FDA, so has USDA a research responsibility in ARS and a regulatory responsibility in APHIS.

Senator BAUCUS. I am not saying they are my thoughts, I am saying that some have those concerns, and from the face of it, those are concerns that one could legitimately have.

Dr. GILLES. Yes, but I think also we must deal with the observation that when we are dealing with life cycles, we need to consider the entire life cycle. To direct our researchers to such a compartmentalized approach that they would only consider one aspect of the life cycle of a plant would, I think, impose unnecessary and undue constraints and, in fact, place us economically and technically at a severe disadvantage.

Senator BAUCUS. I would like to go back to the complexity point. As I recall the problems facing Dr. Strobel, he was operating under essentially NIH guidelines and it turned out that EPA interpreted a certain definition differently than did NIH, as he thought.

He, therefore, assumed that when he contacted the EPA that the EPA would be using the same definition of a substance or process as NIH. It turned out that EPA had a different interpretation than did NIH. That is one complexity that he was caught up with.

In addition to that, if he had waited several days later, then he would also come under, I think, FIFRA, in addition to the other agencies he is dealing with. It seems to me that he has a good case, that is, that this is getting very complex. He has to deal with different agencies. Different agencies have different interpretations. It is a mess.

I can legitimately empathize with that worry that he had and I am sure others have. That is going to be more a problem as biotechnology develops, and as new applications are sent into various agencies or new permits are requested, it is going to accelerate.

As I understand it, I think there are only three uses of microbes that have been permitted by the EPA, and that is only three, I expect many more are going to be utilized and commercially developed in the not too distant future. It just seems to me they have different agencies, different statutes, and that researchers have a very legitimate case of undue, unnecessary complexity and they have a problem.

Don't you agree that they have a problem? There should be some unification, some simplification here? On the face of it, I think that there should be.

Could you explain to me why the present process is not too complex, not too overlapping, and not too difficult for researchers to understand, don't forget, I think, all researchers want to do a good job. They are human beings they live in this country, they don't want to harm the environment, but they are also researchers and they want to develop science consistent with the public safety, and it seems to me they have a good case.

Dr. Moore.

Dr. MOORE. Senator, I don't think there is any question in my mind or in the mind of my colleagues that to the views of the researchers that the rules and requirements may be bewildering, if not befuddling to somebody who doesn't deal with them with great regularity.

I do believe that that should pass to the government, in this case, as well as maybe the organization in which the researcher works, to at least have a single focal point that might be able to help that individual out, to keep them out of trouble.

Also, as you point out, there is no question that there are differences and nuances between the various organizations that are sitting here.

Senator BAUCUS. Some look at process, some look at products, some permits, some don't. It is all very confusing with the different applications.

Dr. MOORE. NIH has elected to focus on recombinant DNA, a specific tool or technique involved in biotechnology. EPA, on the other hand, asserts that it is interested in non-indigenous organisms, no matter how they are made. We are concerned about an organism being put into an environment which is foreign.

Senator BAUCUS. Let me ask the question more precisely. Why shouldn't there be a single agency that deals with biogenetic development?

Dr. MOORE. Simply stated in response, I think, the diversity of products and places where biotechnology is already being brought to bear suggests that it is inappropriate just to have a single biotechnology focus.

The needs and the utility of biotechnology as it might relate to NIH research as contrasted to FDA in the development of new drugs, as opposed to USDA in the development of new plant strains and EPA in the scheme of pesticide development or organisms that might be involved in clean up of concentration of given chemicals, it suggests a diversity of approaches. I am afraid, if you unify it I think one would end up stifling more and making more ponderous progress rather than solving the problems.

Senator BAUCUS. Why not a constitution, if you will, of biological genetically-altered development, or, say, one statute and various agencies apply their processes to that same statute. What is wrong with that?

Dr. MOORE. I think that there probably is merit to an approach that maybe can serve as a uniform reference to all people who are looking towards doing something that involves experimentation into the environment. In essence, I think we have that for experi-

mentation done in the laboratories, since most of the organizations of this country, including sister agencies, have basically suggested that one should follow the NIH or RAC guidelines for the recombinant DNA.

Senator BAUCUS. Dr. Gartland and Dr. Gilles, do you believe that there is merit to the approach of a single statute that different agencies then operate under?

Dr. GARTLAND. I think, Senator, the government attempted with the coordinated framework to put together a structure pulling together all these different regulations and laws to see if it wouldn't work, because the feeling in the different agencies was that they would have adequate authority to do it, and it could be promulgated in such a fashion that it would be understandable. I think it is still a bit of an experiment.

The NIH piece of it was, for historical reasons, focused on recombinant DNA, because the investigators who developed that technique, the pioneers in it, said there might be some concern here, and we should have some special oversight of it. Because of the NIH's mission, we have been primarily focused on biomedical research, the sort of traditional, contained biomedical research, and not in the environmental areas.

Basically, the scientific community has not come forward and said we really need to worry about these other areas, these other areas of biomedical research, in the laboratory setting, so NIH has basically stayed with the definition of recombinant DNA.

Senator BAUCUS. Dr. Gilles.

Dr. GILLES. I would agree, substantially, with the previous commentators.

Senator BAUCUS. About a single statute, under which all agencies operate?

Dr. GILLES. No, sir.

Senator BAUCUS. Why not?

Dr. GILLES. I think, the point that Dr. Moore made is very germane.

Senator BAUCUS. You are saying that it has promise, because that is what he said.

Dr. GILLES. It has promise, certainly. I am not shutting the door on any possibilities, but I think one must recognize that the complexities would certainly prove to be a deterrent and, I think, that that is something that should be kept sharply in focus.

Also, I think, as you deal with the areas of research, while it is true that the research people should ideally be proactive, plan their research and conduct it according to a plan, this is really the general research mode, it is not always done in that manner and, in reading the papers, one would almost think that Dr. Strobel's approach was a reactive approach.

Having spent quite a bit of time as a research administrator at a land grant university, most of the research projects are approved prior to the time they are initiated and this approval usually goes through the head of one's discipline or department. In that area, those people are the ones that should be knowledgeable about the regulations.

Senator BAUCUS. I appreciate it. Our time is kind of limited here.

I still have a problem because, as I understand it, even under the coordinated framework, different agencies have notification differences, the public involvement under the various agencies is different. There are differences in definition, different enforcement mechanisms and penalties.

It seems to me that is a fairly complicated morass, even under the coordinated framework. It may be that there is some coordination, but that doesn't, by any stretch of the imagination, mean that there is not unnecessary complexity. It seems to me, on the face of it, this has to be cleared up and simplified to some degree.

Another question, if you are giving us guidance in how to draft a statute, how would we begin to approach risk assessment, that is, separating the benign developments from those that are potentially dangerous?

Dr. Moore.

Dr. MOORE. Senator, I think, there are documents that have been promulgated recently that shed light in that area. The recently produced report of the National Academy, I think, gives some insight as to things that one should look at or review. I think that the two agencies in the Federal government that often have joint jurisdiction or joint interest into releases into the environment, EPA and USDA, I think, are well on the way of developing a uniform approach as to the factors that one wants to consider in assessing whether or not an experiment should go forward or not go forward based on consideration of proper facts. I think that should be the crux.

What is this paragon, if you will, that one should task themselves to work through in order to reach this judgement that this poses no risk, or this poses modest risk, and which could be controlled or, indeed, it should not go forward?

That Academy document is working that way. I think our Advisory Committee works that way and, as I understand, USDA's process of review, they basically are looking at the same types of factors that we all look at.

Senator BAUCUS. Dr. Gilles.

Dr. GILLES. Again, I agree with Dr. Moore, I think there are several instances where EPA and USDA have shared documents, and have shared responsibilities as far as reviewing.

Senator BAUCUS. I would like you not to define process, just to define substance, that is, what is the approach we should take generally to determine in writing a statute whether certain applications are benign on the face of it?

How do you separate? How do you decide?

What criteria would you suggest for us, so that we could write a statute to adequately address that?

Dr. GILLES. As we approach the plant pest area, we struggled with should we exclude organisms that we thought were not dangerous, or should we include organisms on that list that were dangerous, and we took the inclusive approach rather than the exclusive approach. This is not easy because it opens up the possibility that in the future you may have to add or subtract from that list. Whatever you do should be a dynamic instrument or should provide for a dynamic instrument.

Senator BAUCUS. I must say, it sounds like we really don't have a good handle on this.

Dr. Moore.

Dr. MOORE. If I understand, possibly, the nature of your question, things that one wants to ask in reaching that determination—I don't care who it is that is forming the evaluation—is:

How stable is this organism that we are proposing to use?

How is it going to survive out in the field?

How competitive is it going to be with other organisms or other things that are out there in nature, and is that competitiveness going to provide some deleterious effect?

Post-gains, in addition to whatever it is you might be looking for out there, what else might it do?

Those types of things have been articulated by this Agency and other agencies as to the proper things that need to be looked at in making such a determination.

Senator BAUCUS. I will ask you to submit those criteria for the record, Dr. Moore, if you could?

[The information requested follows:]

DATA REQUIREMENTS FOR REVIEW OF MICROORGANISMS UNDER
TOXIC SUBSTANCES CONTROL ACT AND
FEDERAL INSECTICIDE, FUNGICIDE AND RODENTICIDE ACT
from the
JUNE 26, 1986 FEDERAL REGISTER
COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY

I. Data Requirements under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)

A. Level I Reporting

1. Identity of the microorganism, including characteristics, and means and limits of detection.
2. Decription of the natural habitat of the microorganism or its parental strains, including information on natural predators, parasites, and competitors.
3. Information on the host range of the parental strain(s) or nonindigenous microorganism.
4. Information on the relative environmental competitiveness of the microorganism, if available.
5. If the microorganism is genetically engineered, information should be provided on the methods used to genetically engineer the microorganism(s); the identity and location of the rearranged or inserted/deleted gene segment(s) in question; a description of the new traits(s) or characteristic(s) or characteristic(s) that are expressed; information on potential for genetic transfer and exchange with other organisms, and on genetic stability of any inserted sequences.
6. A description of the proposed testing program, including site location, crop to be treated, target pest, amount of test material to be applied, and method of application.

B. Level II Reporting

1. Background information on the microorganism
   a. Identity of the microorganism, including tables of characteristics, and means and limit of detection using the most sensitive and specific methods available.
   b. Description of the natural habitat of the microorganism or its parental strains, including information on natural predators, parasites, and competitors.
   c. Information on host range, especially infectivity and pathogenicity to nontarget organisms.

d. Information on survival and ability of the microorganism to increase in number (biomass) in the environment (e.g., laboratory or containment facility test data).
e. If the microorganism is genetically altered, the following information should be provided in addition to the information listed in (a) through (d) above:

i. Information on the methods used to genetically alter the microorganism.
ii. The identity and location of the rearranged or inserted/deleted gene segment(s) or characteristic(s) that are expressed.
iii. Information on the control region of the gene(s), and a description of the new trait(s) or characteristic(s) that are expressed.
iv. Information on potential for genetic transfer and exchange with other organisms, and on genetic stability of any inserted sequence.
v. Information on relative environmental competitiveness compared to the parental strain.

2. Description of proposed field test
a. The purpose or objectives of the proposed testing.
b. A detailed description of the proposed testing program, including test parameters.
c. A designation of the pest organism(s) involved (comment and scientific names).
d. A statement of composition for the formulation to be tested, giving the name and percentage by weight of each ingredient, active and inert, production methods, contamination with extraneous micoorganisms, potency and amount of any toxins present, and where applicable the number of viable microorganisms per unit weight or volume of the product (or other appropriate system for designating the quantity of active ingredient).
e. The amount of pesticide product proposed for use and the method of application.
f. The State(s) in which the proposed program will be conducted, and specific identification of the exact location of the test site(s) including proximity to residences and human activities, surface water, etc..

g. The crops, fauna, flora, geographical description of sites, modes, dosage rates, frequency, and situation of application on or in which the pesticide is to be used.
h. A comparison of the natural habitat of the microorganism with the proposed test site.
i. The number of acres, number of structural sites, or number or animals/plants, by State, to be treated or included in the area of experimental use, and the procedures to be used to protect the test area from intrusion by unauthorized individuals.
j. The proposed dates or period(s) during which the testing program is to be conducted, and the manner in which supervision of the program will be accomplished.
k. A description of procedures for monitoring the microorganism within and adjacent to the test site during the field test.
l. The method of disposal or sanitation of plants, animals, soils, etc. that were exposed during or after the field test.
m. Means of evaluating potential adverse effects and methods of controlling the microorganism if detected beyond the test area.

3. Experimental use permits, large-scale testing, and registration
   a. General data requirements for microbial pesticides. The existing pesticide data requirements and regulations govering large-scale field testing (40 CFR Parts 158 and 172) and registration (40 CFR Parts 158 and 162) are applicable to all microbial pesticides, both naturally occurring and otherwise.
   b. Additional requirements for genetically engineered and nonindigenous microbial pesticides.
      1. Description of the natural habitat of the microorganism or its parental strains, including information on natural predators, parasites, and competitors.
      2. Information on relative ability to survive and increase in number or biomass as compared to the parental strains.
      3. Selected environemntal fate tests from 40 CFR 158.170
      4. Additional toxicology tests form 40 CFR 158.170.
      5. If the microorganism is genetically altered, then information on the genetic modification techniques used, the identity of inserted gene segment(s) (base sequence data or restriction enzyme map of the gene), the

control region of the gene(s), a description of the new traits or characteristics that are intended to be expressed, and test to evaluate genetic ability and exchange may be required.

II. Data Requirements under the Toxic Substances Control Act (TSCA)

A. To identify the microorganisms, information is likely to required on
1. Source organisms (e.g., taxonomy, source, reproductive cycle, and capacity for genetic transfer).
2. methods used to manipulate source organisms genetically to obtain the resulting product (e.g., source and function of genetic material to be combined; description of methods for vector construction and introduction, fusion of cells, injection of DNA, etc.).
3. The special functions obtained (e.g., new traits intended to be expressed; selection methods; nature and amount of source genetic material remaining in the product microorganism; genetic stability of new trait).

B. Data required for conducting the risk assessment will vary according to the specifics of each case, but in general will fall into several major categories: information on exposure, environmental fate, and human health and environmental effects.
1. If the microorganisms will be produced in enclosed, commercial-scale facilities, or used solely in physically contained systems, the following information should be included:
a. Production processes (e.g., culture conditions and requirements; sites, methods, and amount of manufacture, processing, storage, and shipment, volume, composition, and disposal of wastes).
b. Workplace exposure and worker practices (e.g., potential for exposure, worker protection practices, and equipment).
c. Containment and possible releases (e.g., potential sources and characteristics of releases, physical containment methods, emergency back-up systems, monitoring, and detection methods in event of a release).
2. In the case of small-scale field tests and other environmental releases, the following information should be included:

a. Purpose and intended effect of application
b. Site of application and surroundings, including geographic, physical, chemical, and biological features.
c. Numbers of microorganisms and methods of application.
d. Containment and mitigation measures (e.g., procedures in event of accidental release, for emergency termination of the application, and to reduce dispersal beyond the site).
e. Monitoring (e.g., detection procedures including their limits, sampling procedures).

3. For field tests and other environmental release, data on environmental fate and effects will be essential. The following information should be included:
   a. General background information on the source organism (e.g., habitat and geographic distribution, interactions with other organisms, involvement in biological cycling processes, potential for genetic exchange in nature).
   b. Test data on the new microorganism itself, indicating its potential for survival, replication, dissemination, and genetic exchange with other organisms.

III. References for further guidance on the kinds of data and information that may be relevant to the evaluation of genetically engineered microorganisms.

A. Milewski, E.A. 1985. Field testing of microorganisms modified by recombinant DNA techniques: applications, issues, and development of "Points to Consider" document. Recombinant DNA Technical Bulletin 8:102-108.
B. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines; Subdivision M-Biorational Pesticides. #PB83-153965, National Technical Information Service, Springfield, VA.
C. Gillett, J., Levin, S., and Stern, A. 1985. Potential impacts of environmental release of biotechnology products: Assessment, regulation, and research needs, Cornell Ecosysstem Research Center, ERC-075, Ithaca, NY.
D. Covello, V.T., and Fiksel, J.R., eds. 1985. The suitability and applicability of risk assesssment methods for environmental applications of biotechnology. National Science Foundation, Report #NSF/PRA 8502286, Washington, D.C.

E. U.S. Environmental Protection Agency. "Points to Consider in the Microorganisms," available from TSCA Assistance Office, Washington, D.C.

Senator BAUCUS. Senator Chafee.

Senator CHAFEE. Thank you, Mr. Chairman.

We have some other witnesses and this isn't going to be the last hearing we are going to have on this, this is a pretty complicated area.

I look forward to hearing the next panel, Mr. Chairman.

Senator BAUCUS. Thank you all very much. We have a lot of questions, but we don't have the time. Thank you very much. We appreciate it.

Our next panel includes primarily those involved in research. Gary A. Strobel, Montana State University, Bozeman, Montana; Dr. John W. Jutila, also from Montana State University; Dr. Larry Moore, Oregon State University in Corvallis; and Dr. James Tiedje, Michigan State University at East Lansing.

Dr. Strobel, it is your turn.

STATEMENT OF DR. GARY A. STROBEL, MONTANA STATE UNIVERSITY

Dr. STROBEL. Thank you, Senator Baucus.

My name is Gary Strobel, and I am the R.G. Gray Professor of Plant Pathology at Montana State University.

Senator BAUCUS. Dr. Strobel, before you begin, I am going to remind each witness that we are going to try to adhere more strictly to the 5-minute rule.

Senator CHAFEE. We have each of your statements, so we know what is in them.

Dr. STROBEL. I have been on the MSU staff for nearly 25 years.

One of the areas of research in which we have engaged for the last 10 to 15 years is that on Dutch elm disease, which is probably the best known plant disease in the United States. The disease is caused by a fungus. It is transmitted by bark beetles.

The methods of control presently consist of cutting trees down, spraying the trees with insecticides or injecting them with fungicides. Nevertheless, we have experienced a continued loss of these trees in the United States over the last 50 years. As a result of the advent of the new genetic-biotechnological science, it has been possible to consider a biological control for this disease. Such biological approaches have also been used and are being considered for use for a number of other plant diseases. It is my feeling that, as a result of nearly 7 or 8 years of work on this biological approach to disease control, we have made some progress.

About 8 years ago, we found a bacterium in the environment which occurs on the leaves of wheat, barley, and lilacs around the world that makes antibiotics that kill the fungus that causes the elm disease. When bacteria are placed into trees, our data show that trees are protected from the effects of the pathogen.

We needed some additional information, namely, does this bacterium survive in the trees, does it move in the trees, and does it protect trees in the field? The way to get this information was to do an experiment wherein we genetically marked the bacterium, for the same reason that one might put a brand on a cow and release it into the forest, a small piece of DNA inserted into the bacterium.

This would allow us to track it through the course of time and space in trees.

This experiment was done in 1981. The modified bacterium was put into many trees. The trees were ultimately put into the field in a small test plot after we had done the proper experiments within the greenhouse. Further tests were done in the early 1980s, and a publication appeared in the late September 1987 issue of the National Academy of Sciences.

We had made the bacterial release in 1982 under the complete guidelines of NIH, that is, the organism was excluded from the NIH rule. Also, the USDA was contacted and they said that they had no regulations or rules governing such a release.

In 1987, we wanted to do an experiment in the field in which we could learn the following: Does the bacterium that is genetically marked survive at minus 40 degrees the kind of temperatures we get in Montana? Does it move in the tree? Does it move to the roots? Does it go into the stems? Does it give protection to the tree from the elm disease fungus when it is injected into the tree?

I knew that the bacterium was already in the field plot, since it was put there 5 years ago. I aslo knew that no USDA rule was being broken and the work was excluded from the NIH rule, however, I was told to contact the EPA. Frankly, I got confused. I thought that they were following the NIH rule. In fact, in June of 1986, they published this set of regulations.

Senator BAUCUS. What is that?

Dr. STROBEL. This is the Coordinated Framework of Regulation of Biotechnology. I have read through this, and I can't understand it, I am sorry.

Their definition of what constitutes a genetically engineered organism is different than NIH's. I understand also, in fact, in talking with the folks at EPA, who have been very kind to me through the course of this trouble, APHIS now has anotner set of rules that were issued in June of this year, which has another set of definitions and these are different than NIH and EPA. At any rate, I assumed that the definitions of NIH applied in 1987 and I was wrong.

At the present time, you can imagine that I feel like a small boy in a house with four grandparents, two parents, and two elder siblings. Either a person is going to rebel or he is going to become a paranoid schizophrenic.

I don't have a team of lawyers to help me. Senator Chafee, you have read some of my recommendations that are here for the record. They suggest that biotechnology regulations need to be reduced and simplified to better reflect our current knowledge base.

I would just finally like to say that we need to have a single document—regulations—to help people in science and industry. We need a single lead agency to handle these regulations. I have been getting calls from all around the country from people asking me who to call in the Federal government to get approval for genetic experiments, and this reflects the confusion that exists.

We do not need a new bureaucracy. I wouldn't vote for that, but I do believe that the National Academy of Sciences' document on releasing organisms with recombinant DNA is a good one to serve as a starting point for new regulations. I think that we need to put together a group of interagency personnel. We need to get some

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people from the scientific community and from the general public who are interested in helping to produce a workable document. We need to get this document widely dispersed and accepted, and then I think people will follow it.

Finally, I am hopeful that we will see the tremendous benefits and blessings of research in the field of biotechnology. It has the potential to solve many problems associated with our growing and complex society, including those of human, animal and plant health, environmental problems, and food production.

The future seems bright for this technology to help America solve some of its economic problems and improve its competitive edge. I think that the Nobel prize that was just given to Dr. Solow at MIT points this out very strongly. New technology improves the competitive edge of any society. Genetic engineering is not something to be feared by the public, but something to be used to bless our land.

Finally, if I wouldn't be out of order, I would like to show you the preliminary results of my experiment.

Senator BAUCUS. Describe it so that everyone in the room can hear what it is.

Senator CHAFEE. Turn around and show it to everybody, maybe they would be interested.

Dr. STROBEL. Both elm trees in this photograph have been inoculated with the fungus that causes Dutch elm tree disease. One of these trees was inoculated with the genetically modified bacterium two weeks before the fungus that caused the disease was placed into the trees. The tree receiving the bacterium was protected. I wish I could have shown you the rest of the trees, namely, there were five other trees in the category that were not pre-inoculated and they all died. There were seven trees in the category that were inoculated with the bacterium and they all survived.

Senator BAUCUS. Would you turn around so that we can see you, too?

Senator CHAFEE. We are anxious for the audience, but why don't you step over there by the television and then maybe we can take care of everybody.

Dr. STROBEL. My Dutch colleagues have picked up on this technology and have inoculated seven to eight thousand trees, north and south, and east to west in Holland. Their data are very promising. I don't say that this is the absolute ultimate elm disease control, but I do say this is something that we need to look at, a direction that we need to go in approaching some of our very severe plant diseases.

Why continue to spray insecticides and fungicides when these very nice, very subtle, very safe biological alternatives exist to handle some serious agricultural, and environmental problems.

Thank you very much.

[A copy of the photograph used by Dr. Strobel at the hearing follows:]

Both American elm trees were afflicted with Dutch elm disease. The tree on the right was treated with a genetically modified baterium. It remained healthy while the tree on the left died.

Senator BAUCUS. Thank you, Dr. Strobel, very much. I am very sensitive to that, too, because I unfortunately had to chop down a Dutch elm in my backyard.

Dr. STROBEL. Did you?

Senator BAUCUS. I had to chop down a Dutch elm years ago.

Dr. Jutila is Vice President of Research at the Montana State University.

STATEMENT OF DR. JOHN W. JUTILA, VICE PRESIDENT, RESEARCH MONTANA STATE UNIVERSITY

Dr. JUTILA. Thank you very much, Senator Baucus and members of the subcommittee.

My name is John Jutila and I serve as Vice President of Research and Professor of Microbiology at Montana State University in Bozeman.

My 31 years of professional involvement in basic research, administration, teaching and public service provide the background for my remarks. Although this has probably been one of the most troublesome issues that I have confronted in my tenure as vice president, I am grateful to have this opportunity to testify before the subcommittee regarding the regulation of biotechnology research.

I do not intend to focus on the specific incident that occurred at Montana State University last summer, about which Dr. Strobel has just briefed you, except insofar as the MSU incident can provide constructive guidance in this review. Indeed, I believe we are fortunate to have had this experience. The incident proved to be without serious negative environmental consequences, and yet it appears to be of sufficient public interest to prompt a review of the policies and procedures involved. Hopefully, the outcome of such a review should be to enhance the performance of a young, but enormously promising field of research and ultimately improve the quality of our lives.

The Montana State University experience demonstrates the need for a rationalization and clarification of the Federal policies and regulations surrounding biotechnology research in general, and those involving recombinant DNA technology in particular.

Dr. Strobel is an internationally known scientist with a distinguished record of research achievement. Yet, even an individual with his experience managed to run afoul of the Federal regulatory system.

It is fortunate that this hearing is occurring on the heels of the recent publication of the National Academy of Sciences entitled "Introduction of Recombinant DNA Engineered Organisms into the Environment," which is a key issue. This document represents the collective judgment of the most respected members of the scientific community and, therefore, our review need not reexamine in great detail the issues already addressed by scholars in this area.

The report deals specifically with the relevant scientific principles and experiences which should govern the decision to introduce into the environment organisms modified by recombinant DNA techniques. Based on a scientific assessment of past experience with the release of genetically altered organisms into the environ-

ment, the committee proposed the formulation of less restrictive scientifically based regulations that stimulate development and uses of such organisms. The findings and conclusions of this report give us guidance with respect to the course of action we must consider for the future.

First, there is need to aggregate existing guidelines from all agencies and offices having a voice in the regulation of biotechnology research. These existing guidelines need to be assimilated into a coherent and comprehensive listing of definition of terms and principles to discriminate among organisms and their release that differ in their potential to cause environmental problems.

The identification of resources and their aggregation into a workable format with a common language would greatly facilitate the development of a policy framework that would serve as a basis for universally accepted guideline. Dr. Strobel has referred to these as a "constitution of biotechnology."

A national commission of knowledgeable persons from the academic community, industry, and government, working in concert with an interagency group should be charged by Congress to develop such a document. Such guidelines may mimic those of the National Institutes of Health and should be reconstructed in accord with the findings and conclusions of the National Academy of Sciences panel.

Second, in response to these universal guidelines, there is need to develop rational policies and procedures for the administration of rules and regulations that emerge from these guidelines.

Third, there is a need to establish an interagency group that assists each regulatory agency with the task of bringing scientific advances into a management scheme in accordance with the universal guidelines. The scientific community at large should provide guidance on a continuing hasis on the redefinition of terms and performance of biotechnology research in general.

Great care should be given to the formulation of policy pertaining to the structure of Federal regulatory mechanisms and their implementation at the local level. We found, in the MSU experience, that the Institutional Biosafety Committee system works very well, and we recommend that the review, evaluation and policing functions of scientific regulation continue to be delegated to the institutions at which the research is occurring, with Federal oversight only of procedures and processes.

In conclusion, there is no question that the caliber of American science would be adversely affected if more restrictive rules and mechanisms of enforcement were implemented by the Federal agencies. I firmly believe that a review of the current regulations and their administrative context would yield an improved system that would continue to facilitate biotechnology research as new knowledge becomes available.

The bottom line, I believe, is an enhanced research environment that helps fulfill the promise of biotechnology research as it pertains to improving human health and the environment.

Thank you.

Senator BAUCUS. Dr. Jutila, thank you very much.

Dr. Moore.

STATEMENT OF DR. LARRY MOORE, PLANT PATHOLOGIST, OREGON STATE UNIVERSITY

Dr. MOORE. Thank you, Senator Baucus, and Senator Chafee.

In the progression of this investigation, some concerns come to me as a scientist.

It has been repeated in a number of instances that biotechnology holds many dangers. I feel a concern about that statement because it may put biotechnology on a par with AIDS, for example, and I see AIDS as far more dangerous.

I feel that to put biotechnology on a par with something like AIDS is, indeed, going overboard. I would say that, in fact, biotechnology may be the instrument or avenue by which we will be able to combat that serious disease.

I am concerned that action should be taken to develop legislation which may become very rigid, and I would urge that any new legislative considerations be very carefully considered.

I would say that my good friend, Dr. Strobel, is one individual who has acted out of frustration. I would also say that hundreds, if not thousands, of other scientists have endured the frustration. It doesn't mean that it is right, or whatever, but since this is part of the focal point of this particular hearing.

I appreciate this opportunity to testify and offer some of my thoughts, opinions, and biases as a scientist on the effectiveness of the current Federal regulations of biotechnology.

I have organized my testimony around several questions. You do not have copies of it. I was notified rather shortly and I just didn't have time to get it ready, but it will be forthcoming.

Number One: Is the present regulatory structure as outlined in various issues of the Federal Register understandable to most scientists?

I say, no. The reason is that it takes a great amount of study because of the complexity of the language, diversity of definition of terms and procedures from one Federal regulatory agency to another, the long length of these documents, and the relatively obscurity of the Federal Register to numerous scientists.

Probably more significantly, is the tremendous amount of scientific publications which scientists should review to stay current with research pertinent to their own field of endeavor. For example, it has been reported that the doubling time for publications in agriculture and biology is two years and even shorter in the area of biotechnology. In short, complex writing which is difficult to read and understand probably gets superficial attention.

Second: Is the present regulatory system or structure inhibiting unduly research and development of biotechnology?

I answer, yes, but with some equivocation. Part of the restrictive regulations has been triggered by, I think, law suits enjoined by advocacy groups who are opposed to the very process of the research in the area of biotechnology, let alone the product of the research.

I think that this has placed pressure on the regulatory agencies to react rather than act. However, in retrospect, perhaps the abnormally long delay of five years to field test Lindow and Penagopolis's Ice-minus strain of pseudomonas syringae wasn't all bad if it

provides us a baseline to compare future requests for environmental release of genetically engineered micro-organisms.

I think the case has been overkill relative to insuring the public safety. It would be a travesty if it became a precedent of procedures required for all future similar releases because of the innocuous nature of this particular genetically engineered micro-organism.

There should be a differential requirement for different levels of risk, with a concomitant reduction in tests over time as field evidence of containment is demonstrated. If not, the consequences of unduly restrictive regulation will be an abandonment of effort by industry to apply biotechnology to commerce. Paradoxically, excessive regulation could also retard efforts of scientists, such as those of Dr. Strobel to provide biological controls to help alleviate some of the problems that have been caused by excessive use of chemical pesticides in the urban and rural environments.

Three: I have been asked at times whether I think the Federal regulatory structure needs to be changed to a single regulatory agency. After some thought, my answer is no. The reason for that answer is that involvement of several agencies provides a diversity of approach to a diverse biology, and a system of checks and balances for the entire biotechnology endeavor.

No one individual or agency is all wise, especially after some years of entrenchment. However, I do favor good coordination among agencies, agreement of definition of the terms, and uniformity of action across agencies. Lines of jurisdiction among agencies should be optimized to prevent instances of double jeopardy and to minimize loss of time during the review process.

In conclusion, I would reiterate that a major concern to scientists is that intellectual endeavor and discovery not be compromised by excessive regulation. Equally important is our societal responsibility to care for the public interest and to provide rational schemes for public safety.

The pivotal question is how these two concerns can be best met? I urge consideration of a prototype of regulatory guidelines similar to that of the NIH RAO guidelines. I have a number of reasons that I would like to read, but in the interest of time, I will not. They will be in the document I will mail to your office. However, I would ask if they could be entered into the record, as well as the National Biological Impact Assessment Program (NBIAP). NBIAP has been proposed by the Cooperative States Research Service and the Biotechnology Committee of the National Association of State Universities and Land Grant Colleges and describes conceptually the idea of a national biological impact assessment program which would be a coordinating body as well as providing regulation.

Senator BAUCUS. Without objection, it will be included.

Dr. MOORE. Thank you.

Senator CHAFEE. Maybe you could just refer to it, if it is pretty long.

Senator BAUCUS. It is not that long.

Dr. Tiedje.

STATEMENT OF DR. JAMES TIEDJE, MICHIGAN STATE UNIVERSITY

Dr. TIEDJE. Thank you, Mr. Chairman, and Senators. I appreciate the opportunity to testify from my experience relative to the regulation of genetically engineered organisms.

My experience with this topic comes from my service on scientific review panels for EPA. I have also worked for 19 years in the field of microbial ecology and I have been editor of the major journal for 11 years that publishes research in microbial ecology.

But I am primarily speaking from my experience with the review of submissions to EPA. I have reviewed 14 submissions to EPA, five from universities and nine from industry, so I was asked to speak relative to my experience of how the current system is working. I would like to go from what I think is successful about the current system, and then what features are not yet optimum.

The first successful feature, I believe, is that the scientific review has been sound. It has been thorough. It has been comprehensive. I believe that that has been adequate and, certainly scientifically credible.

The second feature that has been successful is, from my perspective, the cooperation among agencies has been very good. I would like, as a scientist, to personally thank those agencies and their staffs for that cooperation.

The third point that has been successful is that all interested parties in this debate have had a chance to make their views known and, when their points were appropriate, responded to.

Moving to the features that are not yet optimum, the first one is that the level of review exceeds the risk, from my perspective. Of those 14 submissions that I have reviewed, I would judge them all of low risk. One of them sufficient for an external panel to review because of the unique nature of that particular submission.

I think that the major problem here is that we are still in a new area and, therefore, everyone wants to be careful, be sure that the reviews are thorough, and that public confidence is gained. That is why the reviews have been what I would view as more excessive than justified by the current risk.

I do, however, think, with my experience with EPA over the past two-and-a-half years, that already one sees major signs of progress from the experience gained, such as the last review of the Monsanto pseudomonas lac ZY was much better focused on the relevant issues than certainly the first reviews. So progress is being made, though it is not yet optimum.

The second difficulty is that as it is currently practiced under the coordinated framework, it seems that the level of review for those in industry is a bit higher than those in academia. I think that there is no difference in the relative degree of risk between the sectors in which a person is employed. I think that that needs to be improved.

Senator BAUCUS. Do you mean a more stringent review?

Dr. MOORE. No, equal review. I think that the stringency is more extensive towards those in industry at the present time.

Third is that I would agree that the June 26 Federal Register is difficult to read. I should be a person who has had more familiarity

with that in my service on these panels than others, but I still find it difficult to comprehend. That is part of the problem of a scientist who is not accustomed to reading that kind of information and understanding it. I would appreciate further efforts by the Federal agencies to distill that in a form that is better communicated to the science because I think compliance will be much better if it is more easily understood and can't be missed.

In terms of recommendations, I would agree that the proposal that has come up by two of the previous colleagues that the Institutional Biosafety Committees can he used more effectively in this framework. I think that that has a couple of advantages.

One is that university scientists are accustomed to dealing with institutional committees. We deal with them when we use isotopes, also in human subject research, so it is something that is familiar to us. If that procedure were adopted, I would think that committee should be expanded to include someone with environmental expertise on those committees, though, beyond what they are often constituted.

I think the research could be moved toward a more timely result in the field if those institutional committees could be appropriate.

Finally, one of the important points in why the risk is somewhat uncertain to a lot of people is that we do not have the underpinning scientific information on which to definitively make judgments to conclusively assess that it is low risk. I can do that now, at least in some areas, from my research expertise and from my experience on these panels, but I think that in general one would be more comfortable if one had the underpinning research from which to make general conclusions about risk.

Thank you.

Senator BAUCUS. Thank you, gentlemen.

Dr. Strobel, and you, Dr. Tiedje, the researchers, you are interested in science and the development of science. I think you basically say that the potential risk and danger is not as great as is commonly understood. I think it was you, Dr. Moore, that had that language.

I am wondering if you could more explicitly, more definitely and precisely draw out why you think that the danger is not as great in the development of genetically altered materials as is commonly thought? You say that people compare it with AIDS.

Dr. MOORE. Yes. I see that as far different.

Senator BAUCUS. Would you explain more precisely as to why?

Dr. MOORE. AIDS, as far as its transmission——

Senator BAUCUS. Not so much with AIDS, that is another matter, but just generally.

Dr. MOORE. Let's take Pseudomonas syringae, then, the ice-minus strain. One gene, basically, was altered relative to the wild type. We already have a tremendous amount of data about the wild type. When I say the wild type, I mean those that occur naturally in the environment, and there are billions, trillions over the surface of the earth and on plants.

The loss of that single gene will probably have very little effect upon the survival of the genetically engineered strain. In fact, the data that are now coming out of the experiments from Lindow and the AGS Group in California indicate that they have not been able

to detect it beyond the confines of the small experimental plots which they have established. So I think, from that standpoint, that the strain is very innocuous.

I think that the issue over the ice-minus strain was made regarding the fact that it was engineered genetically rather than focusing upon what it might do as an organism in the environment. Let me say on the other hand that I would not be cavalier in terms of the safety of the public in making such a statement. There may be some severe pathogens of animals. From the veterinary side or even clinical side, that would be more dangerous to the public sector than microorganisms which are associated with the plants. In the case of serious pathogens, there has to be a very careful scrutiny of what we do with those in terms of their release.

I think that the NIH guidelines, as far as laboratory investigations, cover their handling very well. But when it comes to any kind of a release into the environment or into the public domain, we would have to be very careful. I think that almost any scientist you would talk to would have similar feelings to that.

So there is a recognition of differential levels of risk relative to the organism.

Senator BAUCUS. Drawing that out a little bit more precisely, what category of organisms, or what kind of processes, any way you want to define it, is from a researcher's point of view an area that the public should be concerned about?

Dr. MOORE. Where it should be concerned?

Senator BAUCUS. As I understand it, you are saying, and the National Academy of Sciences somewhat recommends, that there is a group of genetically engineered substances that one should not be terribly concerned with, but there is another area that is potentially dangerous. So I am asking you, as a researcher, what kinds of biogenetic developments should we be concerned with?

Where do we start drawing the line from the public's point of view?

Dr. MOORE. I am not going to be familiar with all the kinds of microbes, viruses, et cetera, so I will equivocate on you a bit there, but I will say that I think that those which have been demonstrated to be of low pathogenicity. Some pathogens—I am speaking of plants now because that is my area of expertise—are what we would even call "opportunistic" and, therefore, there has to be a change in the environment to the extent that it will allow them to become infectious, wherein the host is compromised. These become much easier to deal with in terms of pathogens.

There are other strains like rhizobia, for example, which has been released for years and years and years for the beneficial growth of plants we needn't be concerned about, I will be that strong on that, in terms of genetic engineering.

Unless we were to put a gene in it, possibly, which could be transferred to another strain and cause some problems. Generally speaking I don't think that one gene is going to make that big a difference.

Senator BAUCUS. Dr. Strobel and Dr. Jutila, I would like you to address those two questions. The first is: Draw out more precisely why you think, if you do, that the level of review exceeds the risk, or that the problems in developing these materials is not as great

as is commonly thought. The second question is what area do we have to really worry about and focus on.

Dr. STROBEL. I would think that it is going to take much longer than just a few minutes in a hearing such as this to elaborate on these items. But as far as risk is concerned, it would seem to me that uppermost would be genetic experiments done with those organisms that are pathogenic to humans, or animals especially in those cases in which we definitely know that toxins are produced, or, that viral RNA or viral DNA is manipulated. I think that these are areas that need to be closely examined.

However, at the other extreme, as Dr. Moore has pointed out, for us to put regulatory action on organisms that are generally innocuous, such as rhizobia, which is an organism that fixes nitrogen—in fact, 90 percent of the nitrogen that is in my body came from those bacteria that are in the soil associated with legume roots. It seems to me that we need to do everything to enhance, encourage and not to regulate that kind of research, because the alternative is the application of chemical fertilizer.

My recommendation is to start with the Academy report, and with the current regulations and examine these. Then let's throw out the regulations that do not apply and for which there is little or no risk. Let's work together to have a unified and workable framework of regulations.

Senator BAUCUS. Dr. Jutila, do you have any comments?

Dr. JUTILA. Just very briefly, echoing pretty much what Dr. Moore and Dr. Strobel have said.

I dislike generalizing too much, but a release of micro-organisms, whether they are indigenous or non-indigenous, into the environment is really a matter of one question, whether that organism can compete with those that are part of what we call the normal floor of soil or water.

The question that is usually asked is: Will this modified organism compete successfully with its neighbors in that new environment?

My guess is that our greatest danger in this area of biotechnology research and the uses of genetically modified organisms in the area of the human health and animal health—personally I have always felt that the transfer through some new life form, oncogenes or cancer genes, for example, into the human through the injection or ingestion of organisms that are altered genetically in some way. I feel that this is where there should be a strong focus on regulation to avoid some major problems in the human health area.

Senator BAUCUS. This is all very interesting, and I would like to pursue it much more. Unfortunately, we have a time constraint here. I want to thank you all very, very much for participating. Thank you.

Our final panel will consist of Dr. Ronald Meeusen of Rohm and Haas Company; Dr. Rebecca Goldburg of the Environmental Defense Fund; Dr. David Glass of Biotechnica International; and Ms. Anne Hollander of the Conservation Foundation.

Dr. Meeusen, you are first.

STATEMENT OF DR. RONALD L. MEEUSEN, ROHM AND HAAS CO.

Dr. MEEUSEN. I would like to thank the subcommittee for the invitation to testify this morning. My name is Ronald Meeusen and I manage the biotechnology research program for the Rohm and Haas Company.

Rohm and Haas has provided chemical products to the agricultural industry since the 1920s. In the past six decades, we have spent considerable sums of money in research aimed at developing increasingly more cost-effective, safer and more environmentally acceptable products to protect our society's food and fiber crops.

For the last 60 years, that research has principally centered on chemistry because, with a few notable exceptions, biological methods in the past have proven less effective for broad applications in agriculture.

In the late 1970s and early 1980s, however, advances in the biological science began to provide some tools which would, for the first time, allow us to seriously attempt to make effective products based on biology instead of based on chemistry. So Rohm and Haas, like many other companies at that time, began investing in agricultural biotechnology research.

This morning, I would like to review with you one successful outcome of that research investment, which is the development of crop plants which are able to resist insect attack without externally applied insecticides. These recombinant plants were first successfully field tested in 1986, and again in 1987 by the Rohm and Haas Company as one of the first three field trials of genetically engineered plants and served as a test case of the new coordinated framework.

Without going into technical details, let me simply state that under contract to our company, a biotechnology firm in Belgium isolated the gene for a natural, biodegradable, and non-toxic insecticide which has been safely used in this country since the 1960s and moved that gene into plants.

The resulting plants produced minute quantities of that natural non-toxic insecticide in their leaves, effectively killing caterpillars that attempted to feed on the plants. This process is easier to watch than to explain. The short videotape which follows is a time lapse sequence of two plants, one containing the new gene, one not, both infested with the tobacco hornwork caterpillar.

[Showing of the video tape follows:]

Senator BAUCUS. If you could pull that television set around the wall so that everyone in the room can see that?

How long is this?

Dr. MEEUSEN. It is about a one-minute tape, one minute after it starts.

Let me go on with my testimony and give me a high sign when you are ready.

About the time we began to consider field testing these plants, the Federal policy statements of December 31, 1985, appeared in the Federal Register. Since these designated the U.S. Department of Agriculture as the lead agency for plants, we initiated discussions with them early in 1986.

By May of 1986, we had prepared an application for review and approval to conduct field trials at two sites in the south, and sub-

mitted these to the USDA on a voluntary basis. Although formal rules would not be enacted until mid-1987, APHIS took the lead in coordinating their review with the Environmental Protection Agency, and turnaround time for review of this application was about four months. We then were prepared to go ahead with the field test.

However, successful review by the appropriate regulatory agencies was not deemed sufficient grounds at our company at that time to go forward with the trial. We had witnessed public concerns over testing ice-minus bacteria, and so we began a public and regulatory communications program.

Several weeks before we anticipated approval from the agencies, we met with interested parties at the Federal, State and local levels. For both proposed test sites, we briefed staff members of the appropriate Senators and Representatives in Washington. This was followed by visits to the State capitals to meet with representatives of the governors' offices and departments of agriculture and environmental resources, and finally, with local boards of supervisors, the mayors of local cities, and county agricultural extension agents.

To disseminate the information to the general public, seminars were planned in both of the local communities. Invitation lists were compiled from suggestions by State and local officials, and included local farmers, business leaders, and local environmental groups among others. Along with a breakfast briefing, we provided a slide show detailing the project, the planned field work, and the Federal review process.

Reception of this communications program was universally positive. I see the videotape is now ready.

Senator BAUCUS. What is it that we are watching?

Dr. MEEUSEN. What you will be watching here are two tobacco plants. One is a normal tobacco plant, and the other has this gene for the natural insecticide. Both plants have been infested with a dozen newly-hatched Manduca caterpillars placed on the leaves the same way that the adult moth would deposit them. The plant on the left is the normal tobacco, and the one on the right is normal with the one additional gene. The time lapse is about nine days compressed into 60 seconds.

What you will notice if you look very closely at the BT plant, where it seems like nothing is happening, those newly hatched caterpillars did begin to feed, chewed some very small holes, typically a millimeter or two millimeters in diameter, in the leaves, and at that point stopped feeding, crawled to the edge of the leaf and died. While on the other plant these things do what they normally do out in the field, which is eat and eat and eat.

They hatch at about half a milligram, and in 14 days they can get up to ten thousand times their initial weight, and that is why farmers do not like these insects. In 14 days, they can be up as much as five grams in weight, as this insect is if you look at the plant with the control leaves. You can often find the corpus dilecti right near the holes. If you look very closely, you will see the shriveled up body of this small killed insect, and this is entirely in the absence of any kind of applied spray or chemical material.

Both field trials were successful, and sufficiently successful that Rohm and Haas is now investing further research funds to take

this technology out of the test crop and put it into commercial application.

Senator BAUCUS. Are you about finished?

Dr. MEEUSEN. I have other comments, but I will not make them at this time.

Senator BAUCUS. Thank you very much, Dr. Meeusen.

Dr. Goldburg.

STATEMENT OF DR. REBECCA GOLDBURG, ENVIRONMENTAL DEFENSE FUND

Dr. GOLDBURG. Thank you.

I am Rebecca Goldburg. I have a doctorate in ecological biology, and I head the Environmental Defense Fund's biotechnology program. My testimony today focuses on the Coordinated Framework's regulation of releases of genetically engineered organisms, the area of biotechnology regulation of prominent concern to environmentalists.

The coordinated framework is a patchwork, some even call it a crazy quilt, of preexisting statutes loosely stitched together to regulate biotechnology. I have identified 12 ways in which regulation by USDA and EPA, the two agencies that have jurisdiction over most releases, needs improvement. In some cases, agency action or amendments to statutes can correct the problem, but a number of the flaws can only be corrected by new biotechnology legislation.

I will now mention four of the problems discussed in my written testimony. The first two problems are correctable by agency action.

First, USDA notifies the public about a proposed release only after the agency has made a decision about the release. Public participation is limited to commenting on environmental assessment after they are prepared, and scoping meetings for environmental impact statements, when such statements are prepared.

Given the keen public interest in releases, this notification policy is woefully inappropriate. This is especially true since USDA could easily change their policy on public involvement.

Second, concerns about released organisms center around how such organisms will affect native organisms and natural processes. Thus, understanding an engineered organism's ecology is essential to making a decision is essential to making a decision about whether it should be released. Yet, USDA requires no ecological information be submitted to the agency when applying for a permit to release. I don't see how USDA's compliance with NEPA can be credible without such information.

Next, I will mention two problems correctable only by biotechnology legislation.

First, once an engineered organism has passed through TSCA's pre-manufacturing notification process, its use is not restricted, at least not unless EPA implements certain burdensome procedures. Because of the effect an engineered organism has on the environment is a function of the environment that the organism is released into, when, where and in what number an organism is released, will largely determine the associated risks. Thus, it would be far more appropriate for EPA to regulate releases under a stat-

ute written to grant permits for particular applications of engineered organisms, rather than for unrestricted use.

Second, as was mentioned earlier, USDA is an inappropriate lead agency to regulate releases of engineered organisms. This is so for two reasons. First, USDA's mandate is to protect agriculture. Like all agencies, USDA is bound by NEPA, but USDA has no mandate to protect the environment. Even if USDA wants to protect the environment, it has no legal basis for strong regulation.

Second, USDA is in a strange position of promoting the development of agricultural biotechnology while also regulating its products; such divergent goals can only breed internal conflicts. EPA, with a mandate to protect the environment and no vested interest in the development of biotechnology is the obvious lead agency to regulate releases of engineered organisms. USDA's agricultural expertise is absolutely essential for making decisions about releases, but USDA should contribute to rather than be in charge of such regulations.

In conclusion, some of the flaws in the Coordinated Framework, such as USDA's public participation policy, are potentially very easy to correct, others are not, at least not as long as the Coordinated Framework retains its current form. All the flaws are correctable by new biotechnology legislation.

Given the unsatisfactory patchwork nature of the Coordinated Framework, why is there no new biotechnology legislation before us?

First, many individuals have put tremendous effort, some of it very thoughtful and diligent, into crafting the Coordinated Framework from meager starting materials; replacing the Coordinated Framework would mean that that earlier effort is wasted. But this argument also implies that if we are going to replace the Coordinated Framework, sooner is better.

The second reason is related to the first. Now that it is being implemented, there are vested interests in the Coordinated Framework.

I think the third reason is most important. Many people, especially those involved in biotechnology, are afraid of new biotechnology legislation. The mediocre status quo is preferable to the unknown. I find it somewhat ironic that individuals who happily launch themselves into a new technology that may revolutionize many aspects of our private and business lives are frightened by the prospects of new legislation and will tolerate second rate regulation.

We can keep the Coordinated Framework and improve it so that it will always remain the patchwork of statutes with which we decided to make do. I do not believe that this is good regulatory policy.

Thank you.

Senator BAUCUS. Thank you, Dr. Goldburg.

Dr. Glass.

STATEMENT OF DR. DAVID GLASS, BIOTECHNICA INTERNATIONAL

Dr. GLASS. Thank you, Mr. Chairman.

My name is David Glass, and I am Director of Patents and Regulatory Affairs at BioTechnica International. BioTechnica is a six-year old genetic engineering company located in Cambridge, Massachusetts, having its major commercial operations in the areas of agriculture and dental diagnostics, and an advanced research program in production technologies.

Through its subsidiary, BioTechnica Agriculture of Overland Park, Kansas, BioTechnica is developing an agricultural business through technology development, internal growth and acquisition. The company is actively engaged in developing seeds and microbial products enhanced by genetic engineering or other methods, to generate an improved commercial crop. We are primarily targeting the four major field crops of the Midwestern cornbelt: corn, soybeans, wheat and alfalfa.

Our first products are expected to be improved microbial seed additives for increased productivity in the legume crops, alfalfa and soybeans. In fact, earlier this year, we submitted applications to both EPA and USDA proposing our first field tests of such microorganisms, genetically engineered strains of the nitrogen-fixing bacteria rhizobia, which we have heard about already this morning. These are strains of rhizobia which we believe will create yield increases in alfalfa.

This proposal is still undergoing review by the Federal agencies. It was submitted to EPA under their TSCA policy, and to USDA under the regulations under the Plant Pest Act. Details of the conduct of the regulatory review and the status currently of this project can be found in my written statement.

In spite of the fact that our review has not been completed, BioTechnica feels that we can offer some of our own perspectives on the regulatory process, particularly as it has related to our own regulatory review.

Firstly, we believe that the current regulatory framework works in practice. Our experience, and also the experience of several other companies this year, clearly shows that the Federal Government is able to conduct a review of a proposed biotechnology field test under the coordinated framework.

EPA and USDA were able to work together quite adequately in coordinating their reviews, and both agencies were able to work with their counterparts at the State level.

Our proposal was one of the first to go through this process, so clearly there were some things that were not done as efficiently as they could have been. But we have already seen just this week that EPA has already learned from some of the experience that we have gone through in the efficient manner in which they reviewed and approved the field test by Monsanto, which was begun earlier this week.

We have no doubts that, as both the agencies and submitters gain more experience with this process, reviews of proposed field tests can be conducted with the timeliness that is required for agricultural projects without compromising the scientific validity of the review.

Secondly, we believe that TSCA is adequate for the regulation of biotechnology, and that no new laws are needed. No new laws are needed primarily because the expected products of the new biotech-

nologies are so diverse as to necessarily require a product-by-product review under product-specific laws.

More specifically, our experience under TSCA has shown that EPA has the authority to require submission of the data that it needs to complete its review, and that the law is flexible enough to allow the agency to conduct reviews of biological products or proposed biological tests that are appropriate to study the relevant environmental effects.

Thirdly, at this time, the agencies have access to sufficient scientific expertise to conduct their reviews, but this may not be the case in the future if the number of applications significantly increases. Both EPA and USDA were able to call upon sufficient expertise from both inside and outside the agency during the course of their reviews.

However, at EPA in particular, review of the BioTechnica proposal required a considerable allocation of resources, primarily in-house staff. It is not clear whether the agency could possibly simultaneously conduct more than one or two reviews of the scope without taxing their already limited resources.

This point is of particular importance in light of the Montana State incident. The regulatory process cannot possibly continue devoting such inordinate amounts of time and effort to every field test project that is proposed. This level of scrutiny seemed appropriate in the early days of the environmental applications of biotechnology, but the government must develop a means by which the agencies can distinguish the safe ones from the potentially risky ones. This point is especially significant because these initial field tests represent an earlier stage of R&D than is ordinarily regulated by the Federal government.

The government must very carefully balance the need to adequately protect the environment against the danger of unduly hampering innovation by such regulation. It is particularly so where the regulation is singling out one or a small number of research procedures.

The Montana State incident also points out the difficulties in enforcing regulation among the academic community. Companies, even small ones such as ours, expect a certain amount of government regulation and have the staff needed to comply. As we have heard this morning, this is not always the case in universities, and it is clear that the government must adopt regulatory policies that are enforceable and which will be adhered to by the research community.

Let me briefly say that we support a recently proposed tentative proposal, which Dr. Moore made in a speech about two weeks ago, proposing the establishment of environmental biosafety committees patterned after the IBCs of the NIH guidelines.

Senator BAUCUS. Would you wrap up, please, Dr. Glass?

Dr. GLASS. Yes.

Finally, let me just make the last point that central to this or any other scheme to make the process more efficient is the need to distinguish those proposed environmental uses posing low risks from those that have a realistic potential of having higher risks. In this regard, we endorse the concept that the government should regulate the product and not the process.

As has been recently stated by the National Academy report, by focusing on the potential risks of the product, rather than the method by which the product was made, the government can focus more effectively on which products are more risky and which are safer.

I hope that these comments have been helpful, and I will be glad to answer any questions.

Senator BAUCUS. Thank you very much.

Ms. Hollander.

STATEMENT OF MS. ANNE K. HOLLANDER, ASSOCIATE, THE CONSERVATIVE FOUNDATION

Ms. HOLLANDER. Good morning. My name is Anne Hollander, and I am an associate at the Conservation Foundation here in Washington. Prior to that, I served as the first project manager for the biotechnology program implementing the Toxic Substances Control Act for products of genetic engineering.

I really have two major observations I want to make this morning. One is that I think the current system is working reasonably well for now, and I have explained why I think so in my testimony. I think that my colleagues have also explained that for now indications are positive.

Senator BAUCUS. I am sorry but I didn't hear that last statement.

Ms. HOLLANDER. I think for the time being the regulations are working quite well, and that products which have come into the agencies to date have been reviewed fairly quickly and thoroughly. However, I see a number of places in the coordinated framework where improvements are needed. Let me say what some of those are.

I think, first of all, we need to have decentralized reviews for some lower risk products. This has also been stated before. It is really a burden on academic researchers and also a fairly expensive taxpayer burden to have Federal research for every product of genetic engineering.

I think, as we learn more about products, having local level reviews, patterned after the industrial biosafety committee approach, is a very reasonable thing to consider doing, and it is certainly well within the purview of the agencies under their current statutes to implement that kind of a policy.

Something that I am concerned about is that there are some products coming up for which there are no guidelines at all yet. Particularly, I am referring to genetically engineered foods and genetically engineered animals.

The U.S. Department of Agriculture, and the Food and Drug Administration have both indicated that they believe they have responsibility for these areas, but they have not clarified which statutes they are going to use, what they expect the industry to report, and what kinds of risks they are going to be reviewing these products for.

A second issue is that several of the agencies have adopted standards based on the technology, based particularly on recombinant DNA technology, and there are a number of forms of genetic engineering besides that now as there have been in the past.

I don't think that there is a legitimate reason to single-out products of recombinant DNA. In fact, I think that that is an inappropriate approach for two reasons. It is already outdated. Another reason is that it causes economic incentives for the industry and for academic researchers to use other techniques besides the one that is regulated.

I think, in addition, we really need to decide, across the government as a whole, what we are regulating. Are we regulating very novel organisms, or are we regulating certain techniques of genetic engineering? It has been pointed out already today that the coordinated framework is not consistent on this point.

Another concern I have is that the underlying research base on which risk assessments are based, the ecological research base, is going to be strained as more complicated organisms start to be engineered. At the moment, I think that the products that are coming in front of the agencies are fairly straightforward in the manipulations that have been made, and people are using organisms that we have a lot of knowledge about. But that is not always going to be the case, and the underlying ecological research base is not, in my opinion, equipped to handle more sophisticated assessments.

I think that if we are going to aggressively support the development of genetic engineering technology, we need to support the scientific knowledge to understand it and control it. I really think that it is time to think seriously about having some percent of the research dollars, the Federal research dollars that are spent on promoting and building tools of molecular biology, to have some portion of that spent on ecological research so that we can better understand what it is that we are producing.

Another point is that there is some overlapping jurisdiction, especially in the research areas. It is complicated, and I don't want to spend time now describing it, but I think the biggest problems are falling between EPA and USDA in terms of the kinds of things that are going to be subject.

The problem is that the agencies have described their jurisdiction in terms of the funding agency. In instances where research is funded by an agency and by a commercial entity, or perhaps by several agencies, there is no indication at the moment of how or who, mostly who, will regulate that.

My final point is that I really think we need several more years of experience with the regulatory framework before deciding how and whether to build new legislation. The agencies are clearly learning a lot right now as they go through these initial reviews. Neither my comments, nor anyone else's at this hearing, are really based on the kind of research that we need to decide if new legislation is appropriate, especially to decide how to form that legislation.

For that reason, I want to conclude with a suggestion, which is that I think Congress should charge the Federal agencies with commissioning independent empirical studies of how the regulatory procedures are working.

At the moment, natural scientists are taking every opportunity, when an engineered organism is released, to observe it. They consider this a very important chance to gather information about the

scientific aspects of biotechnology. The same thing should be happening on the social science and political science side.

We should be examining how the procedures are working. Some independent study of that should be going on right now so that in a few years, when there is another hearing like this, or sooner, we will have better information than we have now about the kinds of things that may need to he addressed with new legislation and those kinds of things that can be addressed with policy.

Senator BAUCUS. Thank you, Ms. Hollander, for those very thoughtful suggestions.

Let me turn slightly to another subject. What is the competition? What are other countries doing, both in the development of genetic engineering and, second, regulation?

Dr. MEEUSEN. If I may, it varies widely.

Senator BAUCUS. Generally, what is the answer.

Dr. MEEUSEN. From France, where the government has taken an extremely pro-active stance——

Senator BAUCUS. Pro-active in development?

Dr. MEEUSEN. In encouraging development, in investing Federal funds to start up biotech companies, even in agencies offering to run regulatory interference. The company that developed these plants for us, although they didn't have the authority to do this (this in controlled by Rohn and Haas), did receive an offer from an agency official in the French Government to run regulatory interference for the company, draft the documents and get the necessary approvals.

Senator BAUCUS. What are other countries doing?

Dr. MEEUSEN. At the other end of the spectrum, you have countries like Sweden and West Germany, where there is very strong pressure to put an absolute moratorium on any introduction for at least five years. So there is tremendous variation out there.

Senator BAUCUS. What about Japan?

Dr. MEEUSEN. Japan, it isn't really clear yet. MITI is pushing very hard to lay the groundwork to allow these things to be brought in, but simultaneously there is a strong public sentiment to be cautious in moving forward. It is not clear yet what is going to happen.

Dr. GLASS. As I recall, I think Japan has fairly stringent guidelines for contained uses, but nothing in particular on environmental uses.

Senator BAUCUS. I am sorry, I don't know the difference. Do you mean laboratory?

Dr. GLASS. Laboratory and closed production.

Senator BAUCUS. Dr. Goldburg, as I understand, you are suggesting some statutory change. Is that because you don't feel that the present regulatory framework is sufficiently protective of potential adverse risks, or to sufficiently prevent adverse risk; and is it also because you think that there will be a greater number and acceleration of applications that the present framework will not be able to handle?

What is the core problem you have, and what does it all come down to?

Dr. GOLDBURG. I think that there are a number of problems. It is not just one problem. There is a problem with USDA as I cited, the

problem of statutes being used to regulate things that they were not intended to regulate. There is the problem of the speeding up of the number of applications that agencies will receive.

We always have to remember that we are not just developing these regulations for what is going to happen this coming year, when agencies will be facing a few applications, but we are also worrying about application No. 932, when the agencies will have 200 applications to review at the same time.

I think the coordinated framework is deficient in a number of ways. I am also sympathetic to Dr. Strobel's point of view. I am a biologist. I come out of academia. I think the regulations are incredibly confusing. I happen to work for an environmental group so I have attorneys that I can ask questions of, but if I were still at a university, I would feel uncomfortable.

Senator BAUCUS. What about Ms. Hollander's suggestion that it is just too early to draft a statute here? We should charge the agencies with some studies, and so forth, and let this work out a little bit before we try to nail it down more?

Dr. GOLDBURG. I am uncomfortable with that because I think the longer something is around, the more entrenched it gets and the harder it is to dislodge. I think that there is no point in not starting out with the best biotechnology legislation we can up with, and then subsequently modifying that, if we need to.

Dr. MEEUSEN. Mr. Chairman, I think that I would have to disagree with that, and agree with Dr. Hollander. Certainly from our experience with plants, the system is working, and it is working surprisingly well for one of the first three tests going through a new system that has admittedly fairly complex underpinnings to its structure.

Secondly, built into the USDA's approach, and the EPA's as well, if I understand it correctly, are mechanisms to make it flexible so that it can either be made progressively more stringent, if experience dictates that it is needed, or progressively less stringent if the NAS document's projections pan out and, as we gain more experience, we find increasingly large categories that ought be exempted.

I think that we ought to give it some time, because it is structured to self-correct to some degree.

Senator BAUCUS. What about the point that was made several times about the undue complexity. You are an industry, and you can hire attorneys to read all the Federal Registers and try to decipher all this foreign language, whereas a researcher, he can't afford to do that, he hasn't got the time or the resources to do that. Doesn't that cause an undue problem for the university researcher?

Dr. MEEUSEN. I can speak only to plants where I have had the most experience. With plants, where the USDA is the lead agency, it is not too dissimilar from the Tax Code. How many of us really understand the Tax Code. If you have a particularly complicated tax system, if you have lots of investments and other exemptions, you may have to bring in expert help.

I believe that, from our experience, having gone through the process once now, it would be possible for me, if I were at a university, to write USDA under the Freedom of Information Act, if I had a new plant, to get a copy of the expurgated Rohm and Haas, or Monsanto application. Most of the information can be gleaned from

the public literature, and the form is already there. The amount of time and effort, I would estimate I would have to put in, would not be dissimilar to what goes into a typical grant application, which university professors write all the time.

Senator BAUCUS. I will tell you, one of the problems I have is this: Most new ideas, most inventions actually come from small business or individual researchers. They don't come from large institutions, and that is probably because of the bureaucracy.

Dr. MEEUSEN. I agree.

Senator BAUCUS. Large institutions can be stifling. They are not innovative, they like the status quo. They have problems of inertia that are so big that they can't move and change. It is the smaller outfit that basically comes up with more new ideas.

Most new technology comes from individuals who, by definition, because they are smaller, don't have the time or the resources to plow through all of this, the regulations and the complexities and overlap of various agencies.

Dr. MEEUSEN. Absolutely, but the counterpoint of that is virtually every university conducting any recombinant DNA work has an institutional biosafety committee, which should be able to provide some guidance to the individual investigators.

Senator BAUCUS. Dr. Glass, do you want to comment?

Dr. GLASS. It is just an observation. I think, with only a few exceptions, what is clear in the coordinated framework is the product categories. If you have a pesticide, you go to EPA. If you have a drug, you go to FDA. I think that a researcher at either an academic institution or a company, who is developing that sort of a product, would know where to go.

Where the complexity and confusion lies is in the definitions, primarily the definition of what is covered and what isn't. I think that some of the earlier speakers testified to that effect. We believe that this is at least partially due to the fact that, first of all, everybody's definition of biotechnology is different. The government is trying to regulate the process, and not the product.

Senator BAUCUS. Some agencies focus more on the process, and some on the product, as I understand it.

Dr. GLASS. That is right.

Senator BAUCUS. That is confusion.

Dr. GLASS. I am specifically referring to the fact that there are two or three different definitions of what type of organism is covered within a given agency's purview and what isn't.

As Dr. Strobel mentioned earlier, for a researcher who is used to the NIH definition, which is reasonably clear cut, to move toward the other agencies, which may or may not be so clear cut, can be confusing to an academic researcher.

Senator BAUCUS. I very much regret that I have another engagement for which I am 20 minutes late. This has been very, very interesting, and we are only scratching the surface here. I want to thank you very, very much.

It think it is very helpful, and we will probably charge the agencies with buying the kind of studies and materials that Dr. Hollander has suggested.

In addition, I very much agree with Dr. Goldburg, that this is evolving and changing, and we can't wait, which means that I hope

the NIH and various agencies will very aggressively try to simplify and reduce some of the overlap and the complexity, but also in a way that is protective of the public health. They have to keep moving with the times even more aggressively and more quickly than they have. I think they can move more quickly than they have, and we will do our best here to encourage that development.

Thank you very much, we appreciate it.

The hearing is adjourned.

Whereupon, at 12:20 p.m., the subcommittee adjourned.

[Statements submitted for the record follow:]

TESTIMONY OF LUTHER VAL GIDDINGS, PHD
Study Director, Office of Technology Assessment
Congress of the United States
Washington, DC 20510

Hearing on Federal Oversight of Biotechnology Regulation
United States Senate
Committe on Environment & Public Works
Subcommittee on Hazardous Wastes and Toxic Substances
5 November 1987

Good morning. I'm pleased to be here and honored to have been asked to testify.

For more than a year now I have been directing an OTA study to examine scientific issues relevant to planned introductions of genetically engineered organisms into the environment. The report is in the final stages of preparation. Since it has not yet been delivered to the Technology Assessment Board, I am not yet free to discuss in any detail the findings or the issues and options for Congressional Action that form part of the study. There is abundant information available in the public record, however. It is primarily upon this information that I base my comments this morning. I will try to be brief in my remarks so as to leave ample time for questions and for those who will testify after me.

It is no longer news that recombinant DNA and other new biological techniques have brought new vitality to many industries. Researchers can now do much more rapidly many things that used to be prohibitively expensive in time and labor: they can screen large populations of plants or animals for desired genetic characteristics without waiting for mature adults to develop; they can move genetic materially quickly and relatively easily between species where it would previously have been difficult or impossible. They can also now do some new things that were simply not possible before: they can insert specific structural genes or control sequences precisely where they want to, without accompanying genetic material that might complicate the interpretation of results; they can induce precise, site-specific mutations to study the effects of particular changes in gene structure on patterns of gene regulation and the development

of organisms.

The power that that these new capabilities brings for good, the power to improve our quality of life, has been widely publicised, and sometimes oversold. Some people are understandably concerned, however, about the potential for problems that might be associated with these new techniques. Although some disagree, I think these people ask legitimate questions, questions that should be asked.

As part of our study of this issue, we decided that it would be valuable to have precise data on public opinion about biotechnology, and particularly about deliberate releases of engineered organisms. We therefore commissioned a public opinion survey by Louis Harris and Associates. This was a thirty minute telephone survey of a national probability sample of 1,273 American adults, carried out between October 30 and November 17, 1986. We have already published the results of this survey and I am including it as an attachment to my written remarks. I will take the opportunity here briefly to recapitulate some of the results we obtained that are particularly relevant to the issue of planned introductions or deliberate releases. Before I mention any specific findings, however, I must add one important qualifier: in constructing this survey we made no effort to design questions to determine what the public actually does understand, as opposed to what they think they understand. We reasoned that people act on what they think they know regardless of whether or not their understanding is precise or technically or accurate. So we decided to measure perception, as a more broadly useful measure than knowledge per se. I will highlight seven results of our survey. We found that:

1) when faced with the fundamental choice between the risks and benefits to society from continued technological and scientific innovation, a majority of the public (62%) says it feels that the benefits outweigh the risks. In contrast, 28% of the public says it feels that the risks outweigh the benefits.

2) only one in five Americans (19%) say they have heard about any potential dangers of genetically engineered products; when pressed only 12% can actually describe a specific problem they have heard or read about. A larger segment of the public (52%) says it believes that genetically engineered products are at least somewhat likely to represent a serious danger to people or the environment. Nonetheless, a two-thirds majority (66%) says it thinks that genetic engineering will make life better for all people.

3) a majority of the public appears willing to accept relatively high levels of risk to the environment to gain the potential benefits of genetically engineered organisms. 55% say they would approve the environmental use of an organism that would significantly increase farm production if the risk of losing some local species of plants or fish were 1 in 1,000. As the level of risk declines, an increasing number say they would approve of the environmental use of genetically altered organisms for agriculture. However, despite public willingness to approve environmental use of genetically engineered products at relatively high levels of risk, a majority of the public says it would not approve if the risk were unknown. Substantially fewer (45%) say they would approve if the risk were "unknown, but very remote" than if the risk were 1 in 1,000 (55%).

4) a large majority of the public (82%) says it favors environmental applications of genetically altered organisms on a small-scale, experimental basis. In fact, 53% say they would favor and 14% state they would not care if their community were selected as a site to test a genetically altered organism. However, at the time the question was asked only 42% of the public said it

thought commercial firms should be permitted to apply genetically altered organisms on a large-scale basis.

5) in addition to supporting research, the public also sees another important role for government in the development of biotechnology — regulating and assessing potential risks. When asked who should be responsible for deciding whether commercial firms should be permitted to apply genetically altered organisms on a large-scale basis, a plurality said they felt that a government agency should decide (37%). However, the survey also identifies a potential credibility problem in governmental involvement in biotechnology. The public believes that Federal agencies are distinctly less able than university scientists to asses potential risks. Moreover, in disputes between Federal agencies and environmental groups over risk statements, the majority of the public says it is inclined to believe the environmental groups.

6) while the public expresses concern about genetic engineering in the abstract, it says it approves nearly every specific environmental or therapeutic application. And, while Americans find the end products of biotechnology atractive, they are sufficiently concerned about potential risks that a majority say they believe strict regulation is necessary.

7) Finally, while the public expects strict regulation to avoid unnecessary risks, obstruction of technological development is not a popular cause in the United States in the mid-1980s. The survey indicates that a majority of the public says it believes the expected benefits of science, biotechnology, and genetic engineering are sufficient to outweigh the risks.

In conducting our assessment of this topic we have found that there is much that scientists know and understand that is relevant to planned introductions, and much useful experience that can provide guideposts as to how to proceed. But there are also many important uncertainties. Some of these can be addressed by basic research, others only by carefully designed and monitored field tests. And there are a number of questions relevant to regulation. I find it useful to break these down into three categories:

- Questions that are asked,
- Questions that ought to be asked,
- Questions Industry might ask of itself.

Questions that are asked often are asked irrespective of whether or not they are appropriate or useful questions. They often include questions like the following:

- How dangerous/how safe are genetic engineering and biotechnology?
- How risky/safe is it to release genetically engineered organisms? What environmental consequences might there be? What economic consequences?
- How can the government regulate industry so as to avoid risk?

Whether or not the tone of concern or apprehension in these questions is justified, it is an accurate reflection of the feelings of at least a portion of the population, as shown by the data on public perception mentioned earlier.

In addition to questions that are asked, there is the second category I mentioned:

questions that ought to be asked; questions that, by being asked, clarify the useful perspective, the illuminating perspective, the point of view that might help a regulator deal with an issue in a practical manner. Such illuminating questions include the following:

- How does recombinant DNA, or other of the new techniques of modern biotechnology, differ from methods that have been used for decades, centuries, or milennia?

- What can be accomplished with these new techniques that would not have been possible with the older ones?

- Are there unique benefits or problems associated with these new techniques? If there are unique benefits, is it not logical to expect that there might be unique problems? If there are, what might they look like?

- Is there a demonstrable need for regulation specific to the new techniques?

- What are the relative costs/benefits of the new techniques as opposed to the older, established, or classical technologies, many of which are now regulated less than are products produced via these new methods? What costs might be associated with excessive regulation?

Addressing questions such as these can do a great deal to placate public concern and smooth regulatory paths for the products of biotechnology.

I also mentioned a third category of questions — one that it is particularly useful for members of the biotechnology industry to consider. They include:

- What can industry do more effectively to communicate straightforward answers to questions that ought to be asked?

- How can industry avoid stimulating fears about its motivations, which are sometimes perceived as focusing on short term profits with insufficient regard for long term consequences?

- What can industry do to respond to or assuage concerns such as those at the root of fearful questions like those mentioned in my first category, questions that are asked regardless of their utility or propriety?

In closing, although I am limited in what I can discuss from our assessment of these issues I would like to describe, in broad terms, some of our primary conclusions.

Our assessment has found that **while there are reasons to be cautious there is no cause for alarm** at the prospect of planned introductions of genetically engineered organisms into the environment. While support for relevant research, both fundamental and applied, will reduce some important uncertainties, some questions can be answered only with practical experience. Realistic small-scale field tests are likely to be the only way in which some uncertainties about planned introductions can be resolved. Two final points:

- Genetically modified organisms will contribute substantially to improved health care, agricultural efficiency, and the amelioration of many pressing environmental problems that have resulted from the extensive reliance on chemicals in both agriculture and industry.

- The scientific community urgently needs to provide guidance to both investigators and regulators in evaluating planned introductions of modified organisms from an ecological perspective.

These last two points, of course, are taken from the recent National Academy of Sciences position paper on this issue.

I thank you for the opportunity to testify, and I would be happy to respond to any questions you might have.

New Developments in Biotechnology

2 Background Paper Public Perceptions of Biotechnology

CONGRESS OF THE UNITED STATES
Office of Technology Assessment
Washington, DC 20510-8025

[The following has been excerpted from the above-titled report.]

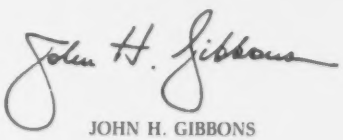
Foreword

Throughout its turbulent recent history, the benefits and risks of biotechnology have been scrutinized and discussed by experts in a wide range of fields. Today, biotechnology is perhaps best viewed as a growing cohort of technologies, each with its own scientific benefits and risks, and allied social, economic, legal, and ethical opportunities and controversies. Increasingly during debates on these concerns, the question is asked: "What does the public think?"

In this background paper, OTA reports the results of a nationwide survey of public knowledge and opinion about issues concerning science and technology in general and genetic engineering and biotechnology in particular. The survey, conducted for OTA by Louis Harris & Associates, measures the interest, knowledge, and concern of the public about scientific matters. The willingness of the American people to accept risks in return for benefits of scientific innovation is assessed. The public's reaction to testing genetically engineered organisms in their own community is reported, as is how the American populace feels about human gene therapy. The background paper also reveals the feelings of the American populace toward the future of biotechnology.

This background paper is the second in a series of OTA studies being carried out under an assessment of "New Developments in Biotechnology." Volume one in the series examined commercia ization and ownership of human tissues and cells, and forthcoming reports will include evaluations of: U.S. investment in biotechnology; genetically engineered organisms in the environment; tests for human genetic disorders; and the impact of intellectual property law on biotechnology. The assessment was requested by the House Committee on Science, Space, and Technology and the House Committee on Energy and Commerce.

OTA was assisted in preparing this study by an advisory panel and reviewers selected for their expertise and diverse points of view. OTA gratefully acknowledges the contribution of each of these individuals. As with all OTA reports, responsibility for the content of the background paper is OTA's alone. The background paper does not necessarily constitute the consensus or endorsement of the advisory panel or the Technology Assessment Board.



JOHN H. GIBBONS
Director

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Chapter 1

Executive Summary

The United States stands at the brink of a new scientific revolution—one based on novel biological techniques—that could significantly alter the lives and futures of many people. While the basic scientific developments that underlie this revolution have occurred already, advances in genetic technology have not yet been applied widely. In the near future, decisions made by the Federal Government will profoundly affect the timing, direction, and limits of this technological revolution—and hence its impact—on the American public. Because government represents all of the public, it cannot ignore the concerns and preferences—no matter the extent of the misconceptions or how transitory the opinions might be—of any portion. It is important for policymakers to know not only what public opinion is, but also on what it is based. But what are the public's perceptions on biotechnology and genetic engineering?

As part of the assessment, "New Developments in Biotechnology," the Office of Technology Assessment commissioned a nationwide survey to answer this question. Conducted by Louis Harris & Associates between October 30 and November 17, 1986, among a national probability sample of 1,273 American adults,[1] this survey gathered information about public knowledge and opinion on science and technology issues in general, and genetic engineering and biotechnology in particular. This background paper presents the data obtained from that survey. It describes **perceptions and beliefs of American adults measured over a 19-day period—public consensus could shift if a cataclysmic event were to occur.**

The survey found widespread interest and concern about scientific and technological issues among the American people. Only about one in six Americans (16 percent) rates his or her basic understanding of science and technology as "very good," and nearly a quarter (23 percent) say that they are "very interested" in scientific and technological matters. And, nearly a third (32 percent) say that they are "very concerned" about government policy concerning science and technology. In all, **nearly half (47 percent) of the adult population of the United States describe themselves as very interested, very concerned, or very knowledgeable about science and technology. OTA defines this population as the science observant public.** Three of ten Americans say they discuss issues related to science and technology at least weekly.

A large majority of the American public (80 percent) says it expects developments in science and technology in the next 20 years to benefit them and their families. At the same time, there is widespread expectation (71 percent) that developments in science and technology will pose at least some risks to them and their families. However, **when faced with the fundamental choice between the risks and benefits to society from continued technological and scientific innovation, a majority of the public (62 percent) feels that the benefits outweigh the risks. In contrast, 28 percent of the public feel that the risks outweigh the benefits.** Neither age, education, nor science observance substantially affects concern about risks of scientific development.

The basic interest in science and technology among the American people carries over to issues of biotechnology and genetic engineering. Two-thirds of the public (66 percent) feel that they understand the meaning of genetic engineering. More than a third (35 percent) say that they have heard or read a fair amount about genetic engineering, yet **only one in five Americans (19 percent) say they have heard about any potential dangers of genetically engineered products. A larger segment of the public (52 percent) believes that genetically engineered products are at least somewhat likely to represent a serious danger to people or the environment.** Nonetheless, a two-thirds majority of the public (66 percent) says it thinks that genetic engineering will make life better for all people.

When all other factors are equal, the public says it is more favorably disposed toward genetic alteration of plants, animals, and bacteria than manipu-

[1] Individuals age 18 and older.

lation of human cells. Approximately one-fourth (24 percent) of the population who have heard about genetic manipulation of DNA to create hybrid plants and animals feel it is morally wrong. Furthermore, 26 percent of the public who are aware of the classic biological techniques of cross-fertilization and crossbreeding also believe that these techniques are morally wrong. This belief opposing any form of biological manipulation, including those in use for thousands of years, is partially a function of religious background. It also reflects a belief that humans should not meddle with nature—a sentiment strongly held by a quarter (26 percent) of the American public.

Some individuals expressed concern about potential risks of environmental applications of genetically engineered products, as well as the moral status of such products. When queried about specific consequences, a majority of the public believes that it is at least somewhat likely that genetically engineered products could create antibiotic-resistant diseases (61 percent), produce birth defects in humans (57 percent), create herbicide-resistant weeds (56 percent), or endanger the food supply (52 percent). Fewer than one in five Americans, however, thinks any of these outcomes is very likely.

A majority of the public appears willing to accept relatively high rates of risks to the environment to gain the potential benefits of genetically engineered organisms. Fifty-five percent say they would approve the environmental use of an organism that would significantly increase farm production if the risk of losing some local species of plants or fish were 1 in 1,000. As the rate of risk declines, public approval of environmental use of genetically altered organisms for agriculture increases. **However, despite public willingness to approve environmental use of genetically engineered products at relatively high rates of risk, a majority of the public says it would not approve if the risk were unknown—substantially fewer (45 percent) say they would approve if the risk were "unknown, but very remote" than if the risk were 1 in 1,000.**

Under conditions of no direct risk to humans and very remote risks to the environment, a majority of the public says it would approve the environmental use of genetically altered organisms to produce disease-resistant crops (73 percent), bacteria to clean oilspills (73 percent), frost-resistant crops (70 percent), more effective pesticides (56 percent), and larger game fish (53 percent). This overall approval, however, is qualified. **A large majority of the public (82 percent) favors environmental applications of genetically altered organisms on a small-scale, experimental basis. In fact, 53 percent say they would favor and 14 percent state they would not care if their community were selected as a site to test a genetically altered organism. However, only 42 percent of the public think commercial firms should be permitted to apply genetically altered organisms on a large-scale basis.**

The issue of human cell manipulation is more sensitive than other forms of genetic engineering. While a majority of the public (52 percent) believes it is not morally wrong to change the genetic makeup of human cells, a significant minority (42 percent) says that it is. When confronted with specific applications of human cell manipulation, however, many Americans relax their position. A large majority of the American public says it approves of scientists changing the makeup of human cells: to stop children from inheriting a usually fatal genetic disease (84 percent); to cure a usually fatal genetic disease (83 percent); to stop children from inheriting a nonfatal birth defect (77 percent); or to reduce the risk of developing a fatal disease later in life (77 percent). In fact, a large majority of Americans (78 percent) says it would be willing to undergo therapy to have genes corrected if tests showed they were likely to get a serious genetic disease later in life. An even larger majority (86 percent) says it would be willing to have their child undergo genetic therapy, if the child had a usually fatal genetic disease.

Much of the public actually supports a type of human gene therapy that scientists are not now advocating. At the present time, all proposals for human gene therapy are restricted to somatic cells—those that affect the characteristics of the patient, but not the patient's ability to pass on such traits to future generations. Yet a majority of the public says it favors the correction of potentially fatal genetic defects in germ line cells (defects that

are passed on to future generations,) as well as somatic cells. **A majority of those who feel human gene manipulation in general is morally wrong nonetheless says it would approve its use in specific therapeutic applications.**

Public support for the development and application of biotechnology is neither uniform nor unequivocal. A third of the public believe, to some extent, that it would be better if humans did not know how to genetically alter cells. Nearly a fifth (18 percent) say they would not approve a proposed application for the environmental release of a genetically altered organism even if the environmental risk were only 1 in 1 million. And 11 percent of the public say they would not approve either somatic or germ line manipulation of human cells, even to cure a disease that is usually fatal. The concerns and preferences of these segments of the population must be weighed against the perception of most Americans that genetic engineering will personally benefit them and their families.

A large majority of the American public (82 percent) believes that research in genetic engineering and biotechnology should be continued. Support for this continued research appears in all segments of the population. In fact, continued research into genetic engineering is supported by majorities of those: who believe human cell manipulation is morally wrong (71 percent); who believe that it is likely that genetically engineered products will represent a serious danger (73 percent); and who feel it would be better if humans did not know how to genetically alter cells (63 percent). This public approval for continuing genetic research spills over into widespread support for government funding of biological research. Despite public concerns about a balanced budget, only 10 percent of the American public say that government funding for biological research should be cut. Forty-three percent of the public believe it should remain the same. Four in ten Americans (40 percent) say that government funding for biological research should be increased. Support for government funding for biological research is bipartisan, with 38 percent of Republicans and 45 percent of Democrats favoring increased funding for this research.

In addition to supporting research, the public also sees another important role for government in the development of biotechnology—regulating and assessing potential risks. When asked who should be responsible for deciding whether commercial firms should be permitted to apply genetically altered organisms on a large-scale basis, a plurality felt that a government agency should decide (37 percent). However, the survey also identifies a potential credibility problem in governmental involvement in biotechnology. **The public believes that Federal agencies are distinctly less able than university scientists to assess potential risks. Moreover, in disputes between Federal agencies and environmental groups over risk statements, the majority of the public says it is inclined to believe the environmental groups.**

In summary, most Americans appear to be pragmatists on the issue of genetic engineering. They are concerned about both the morality and the risks of the technology. **The survey finds that while the public expresses concern about genetic engineering in the abstract, it approves nearly every specific environmental or therapeutic application. And, while Americans find the end products of biotechnology attractive, they are sufficiently concerned about potential risks that a majority believes strict regulation is necessary.** Moreover, the majority of Americans believes that a government agency or an external scientific body should be responsible for deciding about environmental use of genetically altered organisms. At the same time, a majority (55 percent) believes that the risks of genetic engineering have been greatly exaggerated, and 58 percent feel that unjustified fears of genetic engineering have seriously impeded the development of valuable new drugs and therapies.

As in other areas of science and technology, people favor the continued development and application of biotechnology and genetic engineering because they believe the benefits will outweigh the risks. And, **while the public expects strict regulation to avoid unnecessary risks, obstruction of technological development is not a popular cause in the United States in the mid-1980s. This survey indicates that a majority of the public believes the expected benefits of science, biotechnology, and genetic engineering are sufficient to outweigh the risks.**

STATEMENT OF
JOHN A. MOORE
ASSISTANT ADMINISTRATOR FOR
PESTICIDES AND TOXIC SUBSTANCES
U.S. ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS
SUBCOMMITTEE ON HAZARDOUS WASTE AND TOXIC SUBSTANCES
U.S. SENATE

NOVEMBER 5, 1987

I am pleased to have the opportunity to appear before the Subcommittee on Hazardous Waste and Toxic Substances today to discuss the U.S. Environmental Protection Agency's (EPA) regulation of products derived using biotechnology. The responsible regulation of these products is one of my highest priorities and I fully recognize that it is essential that the public have confidence in the process we have established to protect public health and the environment. It is also important that the scientific and regulated communities believe that our review process is credible, equitable, and sound. At the same time, it is important that the development and commercialization of biotechnology products be allowed to proceed in a reasonable and timely manner.

I am here today to describe how EPA's implementation of its statutory responsibilities under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Toxic Substances Control Act (TSCA) provides responsible regulation. Attached as Appendices to this testimony are: (1) tables describing briefly EPA's reviews to date under these two statutes; (2) a

description of penalties for non-compliance under TSCA and FIFRA, and (3) in response to your verbal request, the specifics of the case concerning the experiment conducted by Dr. Gary Strobel of Montana State University.

As you know, EPA is one of the several Federal agencies involved in regulating biotechnology products. In order to present the context in which EPA regulates certain products of biotechnology, I would like to describe briefly the Federal coordinated framework for the regulation of biotechnology, and the philosophy which led to its adoption.

In 1984, the U.S. government, recognizing its responsibility to address issues raised by the use of biotechnology, formed an interagency working group under the White House Cabinet Council on Natural Resources and the Environment. This group examined existing laws and concluded that for the most part, these laws as currently implemented would adequately address regulatory needs in biotechnology.

This approach to regulating biotechnology is based on the recognition that biotechnology encompasses a large and varied collection of techniques and activities, and that the potential products resulting from this technology will cover a wide spectrum of uses. The coordinated framework provides that biotechnology products will be regulated in the U.S. as are products of other technologies, i.e., by the various regulatory agencies on the basis of use. Thus, many agricultural

uses of microorganisms, plants, and animals are regulated by the U.S. Department of Agriculture (USDA) under a variety of statutory authorities; foods, drugs and related items are regulated by the Food and Drug Administration (FDA) under its authorities; microorganisms used as pesticides are regulated by EPA under FIFRA; and microorganisms not covered by other existing authorities are regulated by EPA under TSCA. Examples of the types of uses covered by TSCA include microorganisms used in metal mining, degrading wastes, conversion of biomass for energy, production of proteins and enzymes for non-pharmaceutical purposes, and non-pesticidal agricultural applications such as nitrogen fixation.

A policy statement appearing in the June 26, 1986, Federal Register described the comprehensive federal framework for regulating biotechnology. This comprehensive framework provides a basic network of agency jurisdiction over both research and products.

As part of the coordinated framework described in the June 1986 Federal Register, EPA explained how certain microbial products of biotechnology would be regulated by the Agency. EPA indicated its intention to focus regulatory emphasis on three categories of microorganisms: (1) microorganisms with "new" characteristics or that are new to the environment in which they are intended to be used; (2) pathogens or microorganisms containing genetic material from pathogens; and (3) microorganisms covered by the scope of EPA's policy and used in the environment.

I would now like to describe in some detail how EPA is using its authorities under TSCA and FIFRA to regulate microbial products of biotechnology and to focus its regulatory emphasis on certain groups of microorganisms.

TSCA

TSCA authorizes EPA to acquire information on chemical substances and mixtures of chemical substances in order to identify potential hazards and exposures. The statute gives EPA jurisdiction over the manufacturing, processing, distribution, use and disposal of all chemical substances intended for entry into commerce that are not specifically covered by other statutes. TSCA's applicability to the regulation of microbial biotechnology products is based on the interpretation that microbes are chemical substances under TSCA. The simplified basis for this interpretation is that all substances, living and non-living, have a chemical foundation at the most fundamental molecular level.

Some portions of the policy under TSCA announced in the June 1986 FEDERAL REGISTER require rulemaking for full implementation, others became immediately effective. EPA is currently in the process of developing rules to implement fully the policies proposed in the 1986 notice and we anticipate publishing the proposed rules in early 1988.

I would like to describe briefly the regulatory structure under TSCA and indicate which portions of the policy require further rulemaking.

First, EPA judged that microorganisms constructed using genetic material from dissimilar source organisms (i.e., inter-generic combinations) were most likely to exhibit new combinations of traits. Such organisms were defined as "new microorganisms" and thus, subject to scrutiny under the TSCA section 5 premanufacture notification (PMN) requirements for new chemical substances. This policy became immediately effective upon publication of the June 1986 Federal Register.

Second, EPA announced it would modify the research and development (R&D) exemption provisions of TSCA section 5 so that small quantities of "new" microorganisms used in R&D field trials would not be exempt from PMN requirements, as are other microorganisms and chemicals in this phase of product development. This policy is based on the recognition that microorganisms introduced into the environment have the ability to replicate, increase in number and desseminate from the test plot, unlike traditional chemical substances. The Agency must engage in rulemaking to fully implement this policy. In the June 1986 Federal Register, the Agency requested voluntary compliance from companies planning to conduct field tests of "new" microorganisms until the necessary rulemaking modifies this exemption.

Third, the Agency proposed to use the significant new use rule (SNUR) authority of TSCA section 5 to require that environmental uses of microorganisms that may pose significant potential risks be reported to EPA. In the June 1986 Federal Register, the Agency identified pathogens and microorganisms containing genetic material from pathogens as categories of microorganisms that may pose significant potential risk when released to the environment. The Agency requested compliance by the regulated community on a voluntary basis until the rule is promulgated.

Fourth, we announced that we would collect information on all other microorganisms used for TSCA purposes and released to the environment, but not subject to either the PMN or SNUR policies. To accomplish this, the Agency indicated it would promulgate a rule under the section 8(a) authority. EPA believes that such a reporting rule would provide the Agency with information about the environmental use of microorganisms; this information could be used by the Agency to evaluate its biotechnology program, and if indicated, modify its scope.

The June 1986 Federal Register also indicated that EPA expected to use its section 5(h)(4) authority, where appropriate, to exempt certain "new" microorganisms that it finds will not present unreasonable risks. This policy must also be implemented through the rulemaking process.

Finally, in the June 1986 policy statement EPA pointed out that an existing provision of TSCA, Section 8(e), requires that the Agency be notified immediately by manufacturers if they

discover any substantial risks. The June 1986 Federal Register policy statement contains criteria for reporting under section 8(e).

FIFRA

FIFRA establishes EPA's authority over the distribution, sale, and use of all pesticide products, including microbial pesticides. Indeed, the Agency has approximately 20 years of experience in registering microbial pesticides and was able to draw on this experience in developing its policy for regulating microbial products of biotechnology.

A pesticide can be registered for use only if the pesticide will not cause unreasonable adverse effects to humans or the environment. In order to register a pesticide, an applicant must submit or cite data on subjects such as product composition, human health effects, environmental fate, and effects on nontarget organisms.

Since some of the data necessary for registration must be developed through actual field trials, FIFRA provides for regulation of field testing of a pesticide prior to registration through an "Experimental Use Permit" (EUP).

As part of the EUP process, EPA has developed notification procedures for certain microbial products of biotechnology used as pesticides. In the June 1986 Federal Register, the Agency reiterated the position previously announced in October 1984 that EPA should be notified prior to initiation

of small-scale field testing of genetically altered or non-indigenous microbial pesticides. This policy statement is based on the recognition that microorganisms introduced into the environment have the ability to replicate, increase in number, and disseminate from the test site. Because of these characteristics, EPA feels it is prudent to address certain questions before these microbial pesticides are released to the environment. In this manner the Agency seeks to build a data base on these organisms and to increase public confidence in EPA's ability to assess the products of biotechnology. The Agency is currently in the process of revising the EUP regulations to reflect this interpretive policy.

EPA's current policy for small scale field testing of microorganisms subject to FIFRA provides for two levels of review and attempts to relate extent of review to perceived risk attributes of subject microorganisms. In general, Level 2 review requires the submission of more data and allows for a longer review period than a Level 1 review. The following types of microorganisms are subject to a Level 2 review prior to initiating small scale testing: microorganisms formed by deliberate combinations of genetic material from dissimilar source organisms (inter-generic combinations), microorganisms derived from pathogenic source organisms, and nonindigenous pathogenic microorganisms. The following are subject to Level 1 review: all genetically engineered microorganisms not covered in Level 2 and nonindigenous, nonpathogenic micro-organisms.

I would like now to briefly describe the Agency review process for products of biotechnology that are to be tested or used in the environment. The Agency is dedicated to achieving similar reviews under TSCA and FIFRA. At this time, reviews are conducted on a case-by-case basis.

When a submission for small scale field testing is received under FIFRA, EPA staff evaluate the submission and develop a scientific position. During this process, any potential problems, issues, or significant unanswered questions are identified and the likelihood of significant risk from the proposed field testing is addressed.

Similarly for a submission involving field testing received under the TSCA PMN or SNUR provisions, EPA staff groups assess hazard and exposure, and integrate their conclusions in a coordinated risk assessment.

Intra-Agency workgroups then comment on the positions developed by staff for submissions received under both TSCA and FIFRA. If appropriate, the submission and EPA's scientific position are sent to other Federal agencies for comment. Appropriate State regulatory agencies are contacted in order to alert them to the submission, to discuss EPA's assessments, and to ensure that the Federal and State positions are as consistent as possible.

In some cases, in order to obtain an independent peer review of the Agency's scientific position, to address specific scientific questions raised by the Agency, or to identify any

additional data that may be needed to complete the risk assessment, the submission and the Agency's scientific evaluation are sent to a group of independent scientists constituted as a subcommittee of an Agency advisory group. The Agency has recently established a specific committee, the Biotechnology Science Advisory Committee (BSAC), to advise it on biotechnology issues and BSAC subcommittees have assumed responsibility for these independent scientific peer reviews. Prior to the establishment of BSAC, the FIFRA Science Advisory Panel (SAP) performed this function for genetically engineered microbial pesticides. Several proposed field trials have been reviewed by either BSAC or SAP subcommittees and these groups have endorsed EPA assessments.

At the conclusion of a review, the Agency determines whether the microorganism may be released into the environment. Under both TSCA and FIFRA, this decision is based on the assessment of both the potential risks and the potential benefits of the proposed use of the microorganism. Should the analysis indicate that use of the microorganism may pose unreasonable risks, the Agency has authority under either statute to impose restrictions on its use.

I believe EPA has established a scientific review process that is credible, sound and respected by the scientific community. I feel confident that, because EPA's regulatory mechanism for products of biotechnology is based upon thorough scientific review, it will protect the public health and the environment from unreasonable risks while allowing all of us to reap the benefits of scientific and technological innovations.

APPENDIX A

SUMMARY OF REVIEWS CONDUCTED UNDER TSCA AND FIFRA

This summary describes 16 reviews conducted under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and 5 reviews conducted under the Toxic Substances Control Act (TSCA).

Two of the 5 reviews conducted under TSCA were for environmental testing of modified microorganisms. Three of the 5 involved closed system uses of modified microorganisms.

SUMMARY OF PMNs FOR MICROORGANISMS UNDER TSCA

Testing in the Environment

Applicant; Type of Product	Chronology of Events	Major Issues
BioTechnica ° rDNA addition products ° 2 strains of nitrogen-fixing bacteria to enhance yield of alfalfa ° Rhizobium meliloti	° February 1987; submission received ° March 1987; BSAC subcommittee meeting ° May 1987; preliminary decision to approve test suspension of review to develop consent order ° August 1987; Review suspended for additional two months as Company develops monitoring protocols and background monitoring data ° October 1987; Additional data data and protocols received from Company ° Late 1987; anticipated conclusion of EPA review	° Agency has sufficent data to conclude field test is low risk ° Monitoring methods and protocols from the company are needed ° Consent order ensures test conducted with constraints determined by Agency as necessary and ensures data developed
Monsanto ° rDNA addition product ° product to monitor microorganism under field conditions ° Pseudomonas aureofaciens marked with genes from E. coli	° June 1987; submission received ° August 1987; BSAC subcommittee meeting ° September 1987;prelimary decision to approve test review suspended to develop consent order ° October 1987; review completed ° November 2, 1987; test conducted	° Agency has sufficent data to conclude field test is low risk ° Although not needed prior to this small-scale field test, information on economic impact on water quality testing and dairy product shelf-life is needed to evaluate widespread releases, company developing this information ° Consent order ensures test conducted with constraints determined by Agency as necessary and ensures data developed

SUMMARY OF PMNs FOR MICROORGANISMS UNDER TSCA

Use in Closed Systems

Applicant; Type of Product	Chronology of Events	Major Issues
International Minerals and Chemical Co. ° rDNA addition products ° E.coli engineered to contain human gene for insulin-like growth hormone ° Use as a component in cell culture media	° February 1987; submission received ° May 1987; review completed, product judged to be of low risk, no regulatory action taken	
Company Name Confidential ° addition product ° Bacillus subtilis engineered for enhanced production of a protease ° commercial product (kind and name of product confidential)	° May 1987; submission received ° July 1987; review completed, product judged to be of low risk, no regulatory action taken	
Company Name Confidential ° addition product ° Bacillus engineered for enhanced production of hydrolase ° commercial product (kind and name of product confidential)	° July 1987; submission received ° October 1987; review completed, product judged to be of low risk, no regulatory action taken	

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
AGS Notification		
• rDNA deletion product • INA^- bacteria for frost protection • *Pseudomonas syringae* and *Pseudomonas fluorescens*	• November 1984; Notification received • January 1985; SAP subpanel meets • February 1985; Letter to AGS requesting additional information and an EUP	• Potential adverse effect on plants, insects, weather patterns • Competitiveness of INA^- products and potential to displace INA^+ bacteria
Mycogen (informal review)		
• rDNA addition product • B.t. toxin gene inserted into *Pseudomonas* for insect control; CELLS KILLED	• April 1985; Notification received • June 1985; Mycogen informed that Interim Policy does not apply to their killed product	• Applicability of Interim Policy • Mycogen provided data to substantiate non-viability of their product
USDA Notification		
• Undirected mutagenesis product Two species of fungi to be used to control pest fungi • *Trichoderma viride* and *T. harzianum*	• January 1985; Notification received • April 1985; 90 day clock suspended; EPA requests additional information • May 1985; USDA withdraws notification	• Relative level of risk produced by products of undirected mutagenesis compared to other altered products • The extent of data and information needed (and practical to obtain) on these products for a notification

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SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
AGS EUP ° rDNA deletion product ° INA⁻ bacteria for frost protection of plants ° Pseudomonas syringae and P. fluorescens	° July 1985; EUP application received ° August 1985; receipt announced in Federal Register ° September 1985; public comment received ° September/October 1985; SAP and intra-Agency review of comments ° November 1985; approval announced ° November 1985; Agency sued by Foundation on Economic Trends ° February 1986; outdoor testing of rDNA deletion product disclosed ° March 1986; EPA audits AGS and suspends EUPs ° June 1986; civil complaint issued against AGS for violation of EUP regulations, penalty $20,000 ° July 1986; consent agreement and final order signed, settlement $13,000 ° July 1986; EPA reviews and approves AGS plant pathogenicity retest ° December 1986; AGS submits information on proposed test sites ° February 1987; EPA approves test sites, reinstates EUPs ° March 1987; AGS selects Brentwood site in Contra Costa County to run test ° April 1987; AGS sued, injunction requested, request overruled, strawberry plot vandalized ° April 24, 1987; AGS test INA⁻ bacteria, EPA monitors for aerial dispersion ° August 1987; AGS submits summary of results of field trial ° September 1987; AGS requests EUP amendment to conduct 2nd test at same site, EPA decision expected November 1987	° AGS submitted documentation of findings as requested ° Additional data submitted on competitiveness, plant pathogenicity, and colonization, identification and detection ° Assertions of low risk substantiated by data ° Some plant pathogencity data called into question due to methods used ° EPA reinstatement of EUPs pending test site ° Evaluation of monitoring results to determine whether minimal risk conclusions (based on lab and greenhouse data) were borne out by observation in field ° Field test slightly expanded in acreage, # of plants, # of applications

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Monsanto Notification		
° rDNA addition product ° B.t. toxin gene inserted into Pseudomonas fluorescens for insect control	° January 1985; Notification received ° March 1985; SAP subpanel meeting ° April 1985; letter to Monsanto requesting additional information and an EUP	° Could toxin gene insertion mechanism cause environmental problem ° Possible adverse effects on non-target species
Monsanto EUP		
° rDNA addition product ° B.t. toxin gene inserted into P. fluorescens for insect control	° October 1985; EUP application received ° April 1986; SAP subpanel and other agency review EPA inspection of proposed test site ° May 1986; EPA conducts books and records check, informs Monsanto additional data needed ° September 1986; EPA reviews test protocols submitted by Monsanto for use in development of additional data ° November 1987; EUP review suspended pending receipt of additional data	° Agency reviews data generated by company to address major scientific issues identified in Notification ° Determination of Confidential Business Information status of submission ° Questions of colonization and effects on non-targets not fully addressed by available data
Sands Notification		
° Undirected mutagenesis (uv) product ° Derived strains of Scierotinia sclerotiorum to be used to control plant pests	° May 1986; Notification received ° July 1986; SAP and other agencies review ° August 1986; EPA announces decision - no EUP required	° Relative risk compared to parental strain which is wide host range plant pathogen ° Contingency plans for test termination

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Harman Notification		
° Protoplast fusion product ° Hybrid strains of Trichoderma harzianum to be used to control pest fungi	° June 1986; Notification received ° July 1986; SAP and other agencies review ° September 1986; EPA informs Harman no EUP necessary	° Relative risk compared to parental strains ° Competitiveness and effects on beneficial fungi ° Extent of data and information needed for this type of product
Ecogen (I) Notification		
° Plasmid cured and transconjugant strains of Bacillus thuringiensis varieties kurstaki and azawai to be used to control lepidopteran pests	° May 1986; Notification received ° July 1986; SAP and other agencies review ° June 1986; EPA announces decision - no EUP required	° Applicability of Interim Policy to these products ° Relevance of existing data base on B. thuringiensis ° Probability that plasmid cured and transconjugant strains occur naturally
Ecogen (II) Notification		
° Plasmid cured and transconjugant strains of B. thuringiensis ° Test on potatoes ° Includes new strain active against beetles	° March 4, 1987; Notification received ° April 17, 1987; EPA informs Ecogen no EUP necessary	° Expedited review ° Risk issues similar to submission (I) ° Additional host range risk issue due to new toxin active against beetles
Ecogen (III) Notification		
° B. thuringiensis strains similar to submission (I) ° Test on cotton and vegetables	° March 20, 1987; Notification received ° May 12, 1987; Ecogen informed no EUP is necessary	° Expedited review ° Risk issues similar to submission (I)

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Ecogen (IV) Notification		
° *B. thuringiensis* strains similar to submission (I) ° Test on forest trees	° April 10, 1987; Notification received ° April 27, 1987; EPA informs Ecogen no EUP necessary	° Expedited review ° Risk issues similar to submission (I) ° Additional risk issue due to forest use and exposure to forest non-target organisms ° Uses strains active against Lepidoptera and Coleodoptera
University of Arkansas Notification		
° Herbicidal fungus ° Chemically induced mutant (benomyl-resistant) of *Colletotrichum gloeosporiodes*, an EPA registered product (Collego) ° Use on rice and soybeans to control joint vetch	° April 1987; Notification received ° June 1987; Comments received from USDA/APHIS ° July 1987; EPA informs university no EUP necessary	° Expedited review ° Minor genetic modification using classical chemical-induced mutagenesis, no new genetic information added ° Possible host range changes (microbial herbicides are plant pathogens)
University of California Notification		
° rDNA deletion product ° *Pseudomonas syringae* to be used for frost protection for plants	° December 1984; Notification received ° February 1985; SAP provided comments ° March 1985; letter requesting additional data and an EUP	° Potential adverse effects on plants, weather patterns ° Competitiveness of INA^- products to displace INA^+ bacteria

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
University of California EUP		
° rDNA deletion product ° INA⁻ bacteria for frost protection of plants	° December 1985; EUP application received ° May 1986; EPA inspects test site, participates in public meeting, conducts books and records check ° June 1986; EPA grants EUP ° July 1986; EPA conducts "mock" application with aerial monitoring ° August 1986; University of California and CDFA sued by the Foundation on Economic Trends et. al. experiment postponed pending development of further information ° April 1987; University issued go ahead for experiment ° April 1987; INA⁻ treated potato seed pieces planted ° May 28, 1987; plot vandalized spray application of INA⁻ EPA conducts aerial monitoring	° Agency reviews data generated by applicant to address major scientific issues identified in Notification

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
McNeese Notification		
• nonindigenous protozoa (from Thailand) to control mosquitos • Amblospora aedes	• May 1985; Notification received • July 1985; EPA informs applicant that additional data needed to support notification • August 1985; Notification resubmitted with more information • September 1985; EPA meets with USDA to discuss adequacy of data • October 1985; EPA informs McNeese submitted data inadequate; McNeese also asked to comply with applicable USDA/APHIS requirements • November 1987; EPA review suspended pending receipt of additional information	• The amount of data and information needed (and practical to obtain) to adequately assess risks and determine need for an EUP

APPENDIX B

PENALTIES FOR NON-COMPLIANCE UNDER FIFRA AND TSCA

Since penalties are determined by the facts surrounding a case, it is very difficult to speculate on a penalty without knowing who committed the violation, whether it was a willful and knowing violation, how many times the rule or law was violated, or whether the violator has a history of previous violations, etc.

For the purposes of this Appendix, EPA will attempt to describe the allowable penalties under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Toxic Substances Control Act (TSCA). This assumes that the microorganisms and the individual were covered under the rules or law, and that the individual's actions were violative of a FIFRA or TSCA rule.

FIFRA

Section 14 of FIFRA authorizes EPA to impose both civil and criminal penalties. These penalties are each separated into two applicable classes of individuals:

1. registrant, commercial applicator, wholesaler, dealer, retailer, or other distributor,

2. private applicator (e.g., farmers) or other (e.g., homeowners).

A third class, persons who hold or apply registered pesticides, would most likely not be held liable for these penalties.

Class 1 individuals may be assessed a civil penalty of up to $5,000 per offense. Assuming that EPA can show that a Class 1 individual knowingly violated FIFRA, they shall be guilty of a misdemeanor and be fined no more than $25,000, or imprisoned for not more than one year or both.

Class 2 individuals must receive a written warning from EPA or a citation for their first violation. Subsequent violations may be assessed a civil penalty of not more than $1,000 per offense. Assuming that EPA can show that a Class 2 individual knowingly violated FIFRA, they shall be guilty of a misdemeanor and be fined no more than $1,000, or imprisoned for not more than 30 days or both.

The Class is determined by the individual and their regulatory status. For instance, if a university professor violates FIFRA and she/he is also a registrant of a pesticide, then she/he would be encompassed by Class 1.

TSCA

Section 16 of TSCA authorizes EPA to impose civil and criminal penalties. However, unlike FIFRA, TSCA does not differentiate between types of individuals. Any person who violates TSCA is civilly liable for up to $25,000 for each violation, and each day that a violation continues constitutes a separate violation.

If a person knowingly or willfully violates TSCA, EPA shall in addition to or in lieu of any civil penalty, impose a fine of not more than $25,000 for day of violation, or imprisonment for not more than one year, or both.

APPENDIX C

DR. GARY STROBEL OF THE UNIVERSITY OF MONTANA

In early June of 1987, Dr. Gary Strobel of Montana State University contacted EPA to inquire about the requirements for testing a genetically altered microorganism in the environment. He was informed of the notification requirement and also advised that the experiment should not occur prior to EPA's receipt and review of the data and approval of the test.

By letter dated June 15, 1987, Dr. Strobel requested permission from EPA to commence his experiment testing whether a genetically-altered Pseudomonas syringae strain could be used to control the organism causing Dutch elm disease. At the same time, he submitted pertinent information concerning the proposed field test, as required by EPA's June 1986 biotechnology policy statement. The Agency received Dr. Strobel's letter on June 25, 1987.

On June 18, 1987, Dr. Strobel injected 13 elm trees with the genetically altered microorganism. EPA did not learn that Dr. Strobel had begun the experiment until July 14, 1987, nearly one month after he had injected the trees with the organism.

Thus, by Dr. Strobel's premature actions, the Agency was not able to assess the potential risks to human health and the environment prior to the release of the genetically altered micoorganisms. Fortunately, based upon its review of the available data, EPA had reached an interim conclusion (pending receipt of additional clarifying information) that this particular use of the microorganisms was unlikely to present any significant adverse effects to human health or the environment.

However, EPA will not tolerate any infraction of its policies governing products of biotechnology. Therefore, soon after the Agency learned that Dr. Strobel's experiment was underway, it immediately initiated an investigation to determine whether enforcement actions were appropriate. At the conclusion of that investigation, the Agency communicated its strong disapproval of Dr. Strobel's actions to him and to the President of Montana State University. On August 27, 1987, the Agency sent Dr. Strobel a Notice of Warning under FIFRA, notifying him that he was in violation of the EPA's biotechnology policy. Dr. Strobel is considered a private applicator under FIFRA and as such is not subject to a fine on first offense. Dr. Strobel, along with the University's Institutional Biosafety Committee, was informed that any

future notifications submitted by Dr. Strobel for proposed testing subject the Agency's biotechnology policies must first be approved by the university Institutional Biosafety Committee and co-sponsored by a responsible party.

The attached press release issued at the time the Agency's enforcement actions were imposed provides additional information on the investigation and the Agency's reaction to the incident.

United States
Environmental Protection
Agency

Office of
Public Affairs (A-107)
Washington DC 20460

EPA

Environmental News

FOR RELEASE: THURSDAY, AUGUST 27, 1987

Al Heier (202) 382-4374

EPA RESTRICTS FURTHER GENETIC EXPERIMENTATION BY MONTANA PROFESSOR

The U.S. Environmental Protection Agency announced today that it has placed restrictions on Dr. Gary Strobel of Montana State University in conducting any experiments involving the environmental release of genetically altered pesticides.

The agency informed Dr. Strobel that for a period of one year any notification or application for proposed testing subject to EPA's policy must be cosponsored by the university, a colleague or some other responsible party. In addition, any such applications must be reviewed and approved by Montana State University's Institutional Biosafety Committee (IBC) prior to submission to the agency.

The actions were taken after learning that Dr. Strobel recently innoculated 14 elm trees with a genetically altered microorganism. This action occurred prior to any review of the bioengineered product by EPA. Such a review is prescribed by the agency's policy on small-scale field testing of microbial pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act as set forth in the June 26, 1986, Coordinated Framework for Regulation of Biotechnology. Dr. Strobel was informed of today's action by letter.

"We felt we had no choice but to impose restrictions on Dr. Strobel's experiments in view of his recent actions," said Dr. Jack Moore, EPA's Assistant Administrator for Pesticides and Toxic Substances. "While the agency has concerns that Dr. Strobel conducted tests on the bacterium in the open environment prior to agency review or approval and without any peer review of his planned tests, the action we have taken is the result of his failure to comply with agency

(more)

regulations and policies rather than because of any adverse effect this experiment may have had on the environment or public health."

According to information provided to the agency, Dr. Strobel innoculatec the trees on June 18. The agency received Dr. Strobel's package of data and request for review on June 25 (according to EPA's subsequent investigation, the data were mailed on June 15). In late July, EPA learned that the experiment was underway and immediately conducted an investigation. A review of the data available to the agency (though the data is not entirely complete) indicates that the bacterium should not present any significant adverse effects on the environment or public health.

"EPA is not going to tolerate any infraction of its regulations that govern biogenetic pesticide efforts. If these rules are complied with, this field, with its promise of benefits to society, can be safely regulated," Moore continued. "This agency has a good track record in expeditiously reviewing previous submissions from the academic community well within the 90-day time frame set out in our biotech policy."

In a letter to Dr. William Tietz, President of Montana State University, Dr. Moore said, "In my opinion, IBC's are the backbone of the university oversight system. The role of IBC's and academic institutions in the oversight of genetic research conducted in laboratories has served this country well. Because of the effectiveness of this system, I view this type of system as the preferred mechanism for overseeing academic research involving environmental testing of genetically altered microorganisms. I am very concerned that failures of the IBC system may damage the usefulness of this approach, and lead to the imposition of other more bureaucratic mechanisms that may unwittingly stifle innovation."

EPA's policy for regulating biogenetic pesticides requires persons conducting small-scale field tests to supply data to the agency for a determination as to whether an application for an Experimental Use Permit should be submitted.

In 1986, EPA imposed a fine of $13,000 on Advanced Genetic Sciences, a commercial concern based in Oakland, Calif. The fine was imposed for improperly conducting and reporting outdoor testing of its genetically altered bacterial pesticide, Frostban.

Dr. Strobel is considered a private applicat r under the pesticide law and as such is not subject to a fine on first offense.

R-125

# # #

STATEMENT BY

WILLIAM J. GARTLAND, JR., PH.D.

DIRECTOR

OFFICE OF RECOMBINANT DNA ACTIVITIES

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

NATIONAL INSTITUTES OF HEALTH

BEFORE THE

SENATE ENVIRONMENT AND PUBLIC WORKS

SUBCOMMITTEE ON HAZARDOUS WASTES

AND TOXIC SUBSTANCES

NOVEMBER 5, 1987

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Mr. Chairman and Members of the Subcommittee:

I am pleased to appear before you to discuss the role of the National Institutes of Health (NIH) Recombinant DNA Advisory Committee and the NIH Guidelines for Research Involving Recombinant DNA Molecules in the oversight of recombinant DNA research.

Guidelines for Recombinant DNA Research

The NIH was the first Federal agency to exercise oversight of experiments involving recombinant DNA.

It was some of the scientists closely associated with the development of recombinant DNA techniques who first raised concerns about the technology. Participants at a Gordon Conference on Nucleic Acids in July 1973 sent a letter to the U.S. National Academy of Sciences (NAS) asking the Academy to establish a study committee to consider possible problems posed by recombinant DNA research and to recommend specific actions or guidelines.

The NAS formed a Committee on Recombinant DNA Molecules that issued a report which was published in several journals in 1974. The report recommended that the Director, National Institutes of Health, establish a committee (now the Recombinant DNA Advisory Committee) to (a) oversee a program to evaluate hypothetical risks, (b) develop procedures to minimize the spread of recombinant DNA molecules, and

(c) recommend guidelines to be followed by investigators. In addition, the report recommended that an international meeting be convened to review progress and discuss ways to deal with potential hazards.

The international meeting in February 1975 at the Asilomar conference center in California concluded that most recombinant DNA experiments should proceed provided that appropriate containment is utilized. The conference report made general recommendations for matching levels of containment with levels of hypothetical hazard for various types of experiments. The National Institutes of Health (NIH) was then called upon to translate the broadly based Asilomar recommendations into detailed guidelines for research.

The NIH established the Recombinant DNA Advisory Committee (RAC) in response to the request of the National Academy of Sciences. The RAC held its first meeting the day after the Asilomar conference. There were a series of meetings during 1975 and in early 1976. The original NIH Guidelines were issued on June 23, 1976, and published in the Federal Register on July 7, 1976. The Guidelines specify safeguards to be utilized in the course of experiments. The Guidelines also specify certain administrative requirements under the "Roles and Responsibilities" section.

Approximately two and one-half years passed between the issuance of the original NIH Guidelines in June 1976 and their first major revision in December 1978. The Guidelines as revised in December 1978 incorporated a number of new features. Among them, five classes of experiments, agreed to pose no novel hazards, were exempted from the requirements of the Guidelines for laboratory research. There was a general reduction in the level of containment for most experiments covered by the Guidelines.

Section IV of the Guidelines, dealing with "Roles and Responsibilities," was extensively rewritten to define more clearly the responsibilities of the institution, the principal investigator, the NIH, and the RAC. The revised Guidelines broadened representation on local Institutional Biosafety Committees (IBCs), requiring that individuals not affiliated with the institution be included in the membership.

At the time of the 1978 revision, the membership of the NIH RAC was increased and broadened. Before the revision, the RAC was composed of 14 members, of which 2 were non-scientists. The current RAC consists of 25 voting members, including scientists and non-scientists. Also, representatives of 15 relevant Federal agencies were given non-voting membership on the RAC.

The revised Guidelines specify three classes of actions. Under the so-called "major actions," a mechanism was incorporated for future evolution of the Guidelines. A proposal for a major action, which can be a proposed change in the Guidelines themselves, is first published in the Federal Register for at least 30 days of public comment prior to a meeting of the RAC. The proposed action, together with all written comments received, is taken up by the RAC in open session, and members of the public wishing to speak on the subject are given the opportunity. A recommendation on the proposal is made by the RAC to the Director, NIH, and the final decision of the Director is published in the Federal Register. Using these procedures, modifications in the Guidelines have been made at virtually every RAC meeting since December 1978.

Other major revisions of the Guidelines were issued in January and November 1980, July 1981, April and August 1982, June 1983, November 1984, and May 1986. The history of the Guidelines is extensively documented in the ten volumes of Recombinant DNA Research, published by the NIH.

Under the revisions issued in April and August 1982, Section III of the Guidelines, which specifies containment conditions for covered experiments, was reorganized and greatly simplified. All experiments now fall into one of four classes. Certain experiments continue to require prior review by NIH, certain experiments continue to require

review by an Institutional Biosafety Committee (IBC), certain experiments require notice to an IBC simultaneously with initiation of the experiment, and certain experiments continue to be exempt.

Release Into the Environment

I would now like to summarize the evolution of the Guidelines with regard to release into the environment of organisms containing recombinant DNA molecules. The original version of the Guidelines issued in 1976 specified that five classes of experiments were "not to be initiated at the present time." Among these were experiments involving the deliberate release into the environment of any organism containing a recombinant DNA molecule. In the first revision of the Guidelines in December 1978, this prohibition was retained. However, the 1978 Guidelines permitted exceptions to prohibited experiments provided that the experiments were approved by the Director, NIH, following publication in the Federal Register for comment and review by the RAC. In the April 1982 revision of the Guidelines, experiments that were previously prohibited were placed in a new section of the Guidelines entitled "Experiments that Require RAC Review and NIH and IBC Approval Before Initiation." Included again in this category was deliberate release into the environment of any organism containing recombinant DNA. The procedures for approval remained the same but use of the term "prohibited" was dropped.

The revision of the Guidelines issued in June 1983 incorporated new procedures for approval of field testing under certain specified conditions of certain plants modified by recombinant DNA techniques; these now require review by the RAC Plant Working Group, but no longer by the full RAC, prior to approval by NIH.

In November 1985, a new provision was added to the section of the Guidelines that pertains to experiments that require RAC review and NIH and IBC approval before initiation. That provision stated:

> "If the experiments in this category are submitted for review to another Federal agency, the submitter shall notify ORDA [the NIH Office of Recombinant DNA Activities]. ORDA may then determine that such review serves the same purpose, and based on that determination, notify the submitter that no RAC review will take place, no NIH approval is necessary, and the experiment may proceed upon approval from the other Federal agency."

In August 1987 this provision was revised and broadened to cover all recombinant DNA experiments. It currently reads as follows:

> "Any recombinant DNA experiment which according to these Guidelines requires approval by the National Institutes of Health (NIH), may be sent by the

submitter to the NIH or to another Federal agency that has jurisdiction for review and approval. Once approval, or other applicable clearances, has been obtained from a Federal agency other than the NIH (whether the experiment is referred to that agency by the NIH, or sent directly there by the submitter), the experiment may proceed without the necessity for NIH review or approval. However, any experiment that involves the administration of gene therapy to human subjects (see Section III-A-4 of the Guidelines) may not proceed without prior review by the NIH Recombinant DNA Advisory Committee and NIH approval."

It is anticipated that most experiments involving release into the environment of organisms containing recombinant DNA will fall under the jurisdiction of other Federal agencies.

STATEMENT OF DR. KENNETH A. GILLES
ASSISTANT SECRETARY, MARKETING AND INSPECTION SERVICES
U.S. DEPARTMENT OF AGRICULTURE
BEFORE THE SENATE COMMITTEE ON ENVIRONMENT
AND PUBLIC WORKS, SUBCOMMITTEE ON
HAZARDOUS WASTES AND TOXIC SUBSTANCES
NOVEMBER 5, 1987

MR. CHAIRMAN AND MEMBERS OF THE SUBCOMMITTEE, IT IS A PLEASURE TO APPEAR BEFORE YOU TODAY TO DISCUSS THE DEPARTMENT OF AGRICULTURE'S (USDA) REGULATION OF BIOTECHNOLOGY. IN ORDER TO GIVE THE PUBLIC CONFIDENCE IN THE APPLICATION OF BIOTECHNOLOGY TO AGRICULTURE, IT IS IMPORTANT THAT THERE BE A CLEAR UNDERSTANDING OF HOW BIOTECHNOLOGY IS REGULATED.

BIOTECHNOLOGY OFFERS GREAT POTENTIAL IN MANY AREAS, PARTICULARLY IN THE CONTINUING IMPROVEMENT OF OUR CAPACITY TO DEVELOP PRODUCTS THAT ARE OF CRITICAL IMPORTANCE TO THE FUTURE OF AMERICAN AGRICULTURE. IT IS VITAL THAT PRODUCTS OF BIOTECHNOLOGY BE REGULATED BASED ON FIRM SCIENTIFIC PRINCIPLES AND MEET THE SAME HIGH STANDARDS OF SAFETY AND EFFICACY, AS DO THOSE PRODUCTS MADE THROUGH CONVENTIONAL TECHNOLOGY. THUS, WE SEEK TO FOSTER A REGULATORY CLIMATE THAT ENCOURAGES INNOVATION, DEVELOPMENT, AND COMMERCIALIZATION OF BENEFICIAL NEW AGRICULTURAL PRODUCTS DERIVED FROM BIOTECHNOLOGY, WHILE IMPLEMENTING A RESPONSIBLE POLICY THAT LIMITS POTENTIAL OR REAL RISKS. WE REGULATE PRODUCTS BECAUSE OF THEIR POTENTIAL RISK TO PLANT OR ANIMAL HEALTH, AND OUR REGULATIONS APPLY EQUALLY TO EVERYONE CONDUCTING ACTIVITIES COVERED BY THE REGULATIONS.

RESEARCH ACTIVITIES WITHIN THE DEPARTMENT ARE THE RESPONSIBILITY OF THE ASSISTANT SECRETARY FOR SCIENCE AND EDUCATION. USDA AGENCIES MOST DIRECTLY

INVOLVED IN BIOTECHNOLOGY RESEARCH ARE THE AGRICULTURAL RESEARCH SERVICE AND THE COOPERATIVE STATE RESEARCH SERVICE. REGULATORY RESPONSIBILITY HAS BEEN DELEGATED TO MY POSITION--THAT OF ASSISTANT SECRETARY FOR MARKETING AND INSPECTION SERVICES.

COORDINATION OF BIOTECHNOLOGY ACTIVITIES WITHIN USDA IS ACCOMPLISHED THROUGH THE COMMITTEE ON BIOTECHNOLOGY IN AGRICULTURE (CBA), CO-CHAIRED BY DR. ORVILLE BENTLEY, THE ASSISTANT SECRETARY FOR SCIENCE AND EDUCATION AND ME. THE CBA FUNCTIONS AS A POLICYMAKING AND COORDINATING BODY FOR JURISDICTIONAL MATTERS WITHIN THE DEPARTMENT. THE CBA MEETS EVERY 2 MONTHS TO DISCUSS AND RESOLVE SCIENTIFIC AND POLICY ISSUES. IT REPORTS TO THE SECRETARY OF AGRICULTURE ON INTERNAL MATTERS, AND TO THE BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE (BSCC) ON MATTERS OF OVERALL FEDERAL POLICY FOR BIOTECHNOLOGY.

THE OFFICE OF AGRICULTURAL BIOTECHNOLOGY (OAB) PROVIDES STAFF SUPPORT FOR THE CBA. IT ALSO SERVES AS A FOCAL POINT ON BIOTECHNOLOGY WITHIN THE USDA, THUS ASSURING PROGRAM COORDINATION.

THE BIOTECHNOLOGY AND ENVIRONMENTAL COORDINATION STAFF (BEC STAFF) WITHIN THE ANIMAL AND PLANT HEALTH INSPECTION SERVICE (APHIS) COORDINATES THE DEPARTMENT'S BIOTECHNOLOGY REGULATORY ACTIVITIES. THE BEC STAFF ALSO TAKES THE LEAD IN LIAISON BETWEEN APHIS AND OTHER FEDERAL AGENCIES ON BIOTECHNOLOGY REGULATORY MATTERS.

FROM MY PERSPECTIVE, ONE OF THE MANY POSITIVE DEVELOPMENTS IN THE IMPLEMENTATION OF FEDERAL BIOTECHNOLOGY POLICY HAS BEEN THE ESTABLISHMENT OF A COORDINATED EFFORT WITH OTHER FEDERAL AGENCIES, PARTICULARLY THE ENVIRONMENTAL PROTECTION AGENCY AND THE FOOD AND DRUG ADMINISTRATION. USDA SHARES

JURISDICTION WITH BOTH THESE AGENCIES, AND WE WILL CONTINUE TO COORDINATE OUR EFFORTS WITH THEM IN THE FUTURE AS GENETICALLY ENGINEERED ORGANISMS AND TRANSGENIC ANIMALS ARE TESTED AND MARKETED. COORDINATION AND CONSULTATION HAVE ALREADY BEEN DEMONSTRATED WITH JOINT REVIEWS OF APPLICATIONS BETWEEN EPA AND APHIS, AND THROUGH COMMITTEE ACTIVITIES AND INDIVIDUAL CONTACTS AMONG SCIENTISTS.

USDA, ALONG WITH OTHER FEDERAL AGENCIES, STATED ITS POLICY FOR REGULATING BIOTECHNOLOGY IN DECEMBER 1984 AS A PART OF THE "COORDINATED FRAMEWORK." THE USDA POLICY IS FOCUSED ON THREE MAIN ELEMENTS:

- o THE EXISTING STATUTES ARE ADEQUATE FOR REGULATING THE PRODUCTS OF AGRICULTURAL BIOTECHNOLOGY;
- o USDA DOES NOT ANTICIPATE THAT SUCH PRODUCTS WOULD DIFFER FUNDAMENTALLY FROM THOSE PRODUCED BY CONVENTIONAL METHODS;
- o THE PRODUCT AND THE RISK SHOULD BE REGULATED, RATHER THAN THE TECHNOLOGY.

THE USDA CARRIES OUT ITS REGULATORY RESPONSIBILITY UNDER A VARIETY OF AUTHORITIES. STATUTES ADMINISTERED BY USDA AND APPLICABLE TO THE REGULATION OF BIOTECHNOLOGY WERE LISTED IN THE USDA POLICY STATEMENT. THE USDA AGENCIES ADMINISTERING THESE STATUTES ARE APHIS, THE FOOD SAFETY AND INSPECTION SERVICE, AND THE AGRICULTURAL MARKETING SERVICE. BECAUSE APHIS HAS BEEN THE MOST ACTIVELY INVOLVED TO DATE IN REGULATING THE TESTING AND DEVELOPMENT OF GENETICALLY ENGINEERED ORGANISMS, I WILL FOCUS MY COMMENTS ON THE APHIS EFFORT.

APHIS HAS REGULATORY AUTHORITY OVER THE RELEASE INTO THE ENVIRONMENT OF ANIMAL

AND PLANT PATHOGENS, INCLUDING CERTAIN GENETICALLY ENGINEERED ORGANISMS. THE ACT OF FEBRUARY 2, 1903 APPLIES TO THE RELEASE OF GENETICALLY ENGINEERED ORGANISMS WHICH MAY BE ANIMAL PATHOGENS.

VETERINARY BIOLOGICAL PRODUCTS ARE REGULATED UNDER THE VIRUS-SERUM-TOXIN ACT (VSTA) OF 1913. AMENDMENTS TO THE VSTA CONTAINED IN THE FOOD SECURITY ACT OF 1985 EXPANDED APHIS' AUTHORITY OVER VETERINARY BIOLOGICAL PRODUCTS AND GAVE USDA ADDITIONAL ENFORCEMENT MECHANISMS SUCH AS THE POWER TO DETAIN AND SEIZE PRODUCTS. APHIS PUBLISHED FINAL REGULATIONS IMPLEMENTING THE 1985 AMENDMENTS DURING THE SPRING AND SUMMER OF THIS YEAR. THESE REGULATIONS STRENGTHENED AND IMPLEMENTED APHIS' EXPANDED AUTHORITY AT A CRITICAL TIME IN THE DEVELOPMENT OF VETERINARY BIOLOGICS PRODUCED BY RECOMBINANT DNA TECHNOLOGY.

APHIS ISSUES U.S. VETERINARY BIOLOGICAL PRODUCT LICENSES AFTER SATISFACTORY COMPLETION OF ALL REQUIREMENTS, WHICH ARE DESIGNED TO ENSURE THAT THE PRODUCT IS PURE, SAFE, POTENT, AND EFFICACIOUS. VETERINARY BIOLOGICAL PRODUCTS PRODUCED BY RECOMBINANT METHODS ARE EVALUATED ON A CASE-BY-CASE BASIS USING THE SAME STRINGENT STANDARDS FOR LICENSING EMPLOYED FOR CONVENTIONALLY PRODUCED BIOLOGICS.

FOR VETERINARY BIOLOGICAL PRODUCTS THAT ARE RECOMBINANT-DERIVED OR DERIVED FROM MONOCLONAL ANTIBODIES, A THREE-CATEGORY CLASSIFICATION SCHEME BASED ON BIOLOGICAL CHARACTERISTICS AND SAFETY CONCERNS WAS PUBLISHED IN THE FEDERAL REGISTER AS A PART OF THE FINAL USDA POLICY STATEMENT ON BIOTECHNOLOGY IN JUNE 1986. TO DATE, APHIS HAS ISSUED 21 PRODUCT LICENSES FOR PRODUCTS MANUFACTURED FROM BIOTECHNOLOGICAL PROCESSES. ONE OF THESE PRODUCT LICENSES WAS FOR A RECOMBINANT-DERIVED MODIFIED LIVE VIRUS PSEUDORABIES VACCINE. SINCE THE GRANTING OF THE INITIAL PSEUDORABIES VACCINE PRODUCT LICENSE, APHIS HAS

GRANTED AUTHORIZATION FOR FIELD TRIALS IN SUPPORT OF LICENSE APPLICATIONS FOR TWO OTHER RECOMBINANT-DERIVED MODIFIED LIVE VIRUS PSEUDORABIES VACCINES. THE APHIS SAFETY REVIEW PROCESS INVOLVING PRODUCTS CONTAINING RECOMBINANT-DERIVED MODIFIED LIVE ORGANISMS INCLUDES AN ENVIRONMENTAL ASSESSMENT FOR ALL FIELD TESTS AND LICENSING ACTIONS. THE AVAILABILITY OF ENVIRONMENTAL ASSESMENTS IS ANNOUNCED TO THE PUBLIC BY PUBLICATION IN THE FEDERAL REGISTER.

APHIS HAS USED ITS STATUTORY AUTHORITY UNDER THE FEDERAL PLANT PEST ACT AND THE PLANT QUARANTINE ACT TO IMPLEMENT A NEW RULE FOR GENETICALLY ENGINEERED ORGANISMS WHICH ARE OR MAY BE PLANT PESTS. THE FINAL RULE, WHICH TOOK EFFECT ON JULY 16, 1987, ESTABLISHED PERMIT AND OTHER REQUIREMENTS FOR THE IMPORTATION, INTERSTATE MOVEMENT, AND RELEASE INTO THE ENVIRONMENT OF GENETICALLY ENGINEERED ORGANISMS AND PRODUCTS THAT ARE OR MAY BE PLANT PESTS. PRODUCTS ARE REGULATED FOR THEIR POTENTIAL RISK IF THE PRODUCT CONSISTS OF OR CONTAINS AN ORGANISM LISTED AS A PLANT PEST IN THE FINAL RULE. A PRODUCT MAY ALSO BE REGULATED IF THE PRODUCT CONTAINS AN UNCLASSIFIED ORGANISM, OR AN ORGANISM WHOSE CLASSIFICATION IS UNKNOWN, OR ANY OTHER PRODUCT PRODUCED THROUGH GENETIC ENGINEERING WHICH THE AGENCY DETERMINES IS A PLANT PEST OR HAS REASON TO BELIEVE IS A PLANT PEST. THE RULE REQUIRES THAT WE NOTIFY AFFECTED STATES SO THAT THEY MAY REVIEW PERMIT APPLICATIONS. ALTHOUGH THE RULE WAS PUBLISHED AS A FINAL RULE, IT IS FLEXIBLE ENOUGH TO BE AMENDED WHENEVER NECESSARY AS IS REFLECTED IN THE PROVISION ALLOWING FOR PETITIONS TO AMEND THE LIST OF REGULATED ORGANISMS. IN ADDITION, WE HAVE ALREADY PUBLISHED A PROPOSED CHANGE IN THE RULE TO REMOVE CERTAIN RESTRICTIONS AGAINST INTERSTATE MOVEMENT OF CERTAIN MICROORGANISMS UNDER SPECIFIED CONDITIONS WHICH WOULD PROVIDE ADEQUATE SAFEGUARDS TO PREVENT THE INTRODUCTION AND DISSEMINATION OF PLANT PESTS.

SINCE THE FINAL RULE TOOK EFFECT, APHIS HAS RECEIVED 24 APPLICATIONS FOR MOVEMENT AND 6 FOR ENVIRONMENTAL RELEASE OF PLANT ORGANISMS. FOR EACH APPLICATION FOR RELEASE INTO THE ENVIRONMENT, APHIS PREPARES AN ENVIRONMENTAL ASSESSMENT ACCORDING TO THE REQUIREMENTS OF THE NATIONAL ENVIRONMENTAL POLICY ACT.

ANYONE WHO VIOLATES OUR REGULATIONS ON PLANT PESTS, VETERINARY BIOLOGICS, OR ANIMAL PATHOGENS IS SUBJECT TO A RANGE OF ADMINISTRATIVE, CIVIL, AND CRIMINAL PENALTIES.

WE ARE CONFIDENT THAT WE ARE MEETING OUR RESPONSIBILITIES IN A WAY THAT WILL MAKE THE PRODUCTS OF BIOTECHNOLOGY AVAILABLE TO OUR AGRICULTURAL COMMUNITY AS QUICKLY AS POSSIBLE WHILE ENSURING THAT FULL PROTECTION IS PROVIDED TO AGRICULTURE AND THE ENVIRONMENT.

THIS CONCLUDES MY PREPARED STATEMENT, MR. CHAIRMAN. I WILL BE HAPPY TO RESPOND TO ANY QUESTIONS.

Gary A. Strobel
R. G. Gray Professor
Dept. of Plant Pathology
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DOCUMENT FOR SENATE HEARINGS

I am Gary A. Strobel, R. G. Gray Professor of Plant Pathology at Montana State University. I have held various professorial positions at MSU for nearly 25 years. My field of study concerns various biochemical aspects of the diseases of plants. In trying to do a relatively small field experiment on a potential biological control agent of Dutch elm disease, I ran afoul of federal regulations and of the MSU biosafety committee. I have come here to share the details of my experience and to recommend that improvements be made in the manner in which the federal government is regulating this promising field of biotechnology. I also would like to suggest that many of the current regulations do not reflect our current status of knowledge accommodating both the public good and scientific progress.

In order to proceed properly, I feel that it is critical to present some background information on the biological system that is being studied. The Dutch elm disease (caused by the fungus Ceratocystis ulmi) is known throughout North America and Europe as one of the most destructive killers of elm trees. It is probably the best known plant disease in America. It has been estimated that over 1/2 of the ornamental and landscape elms in

the USA, numbering in the millions, have been destroyed by this pathogen. In fact, one elm that graced Capitol hill and witnessed the passage of the majority of this nation's history was killed in 1980 by the Dutch elm disease. The fungus was, to the best of our knowledge was introduced to the US via imported elm logs containing bark beetles coming from Europe. It spread by a bark beetle vector from its initial outbreak in Ohio in 1930, to virtually the entire US by the mid 1980s. Current control measures consist of sanitation practices (cutting down trees), spraying with polluting insecticides to control its beetle vector, or injecting toxic fungicides into the tree.

We started studies on an alternative biological control measure about 10 years ago with funding from the Freshwater Foundation in Navarre, MN. Such a biological control measure would be effective and environmentally safe. We discovered that certain strains of the bacterium Pseudomonas syringae (found on leaves of various plants around the world) produced antibiotic substances that effectively inhibit and kill the fungus[1]. It was demonstrated that some of these bacterial strains were effective against all strains of the fungus. Since the bacteria would grow on elm sap and in elm seedlings it was reasonable to think that they would protect the plant from the effects of Dutch elm disease. This hypothesis and subsequent research eventually led to major field testing of the bacterium in the early 1980s by the Ortho Division of Standard Oil of California in various parts of the U.S. The Ortho people were valiant in their efforts to make

the bacterium perform at the field level, but with little success. In 1982, a Dutch worker (Dr. R. Scheffer of the Willie Commelin Scholten in Baarn, Holland) using native Dutch strains of the bacterium showed that it was essential to have the protective bacterium in the tree before being challenged with the fungus[2]. Also, it was essential to have active/viable cultures of P. syringae and to place them directly beneath the bark with a specially designed tool (gouge pistol)[2]. None of these criteria had collectively been met with the earlier U.S. tests. The Dutch workers now have 5 years of data on thousands of elms and their results give us reason to be optimistic. Later field work in the U.S. begun by C. Murdoch at the Univ. of Maine, on American elms, also showed promising results[3].

In May, 1987, a report of our bacterial genetics/Dutch elm disease work was accepted for publication in the Proceedings of the National Academy of Sciences. It showed that an antibiotic producing strain of the bacterium was capable of protecting small-greenhouse elms from the devastating effects of Dutch elm disease. This bacterium was a mutant strain of P. syringae that had been produced through transposon mutagenesis by Drs. Steve and Brenda Lam using the transposon TN903[4]. The mutant was a slight overproducer of the antibiotic substance which kills the fungus. The presence of the transposon in the bacterium allows it to grow on an agar medium containing the antibiotic kanamycin. Furthermore, since the transposon marker (DNA) in the bacterial chromosome allows the organism to be positively

identified it would be extremely useful in tree studies.

At this point we had shown the protective effects of the bacterium on greenhouse elms, its maintenance in elms over 2 years, and the need of the bacterium to produce antibiotic substances to be effective in protecting trees. The questions which needed answers were: 1) does the bacterium move in the tree?, 2) does it overwinter in the tree?, 3) does it offer any protection to the tree in the field to the fungus? I needed to acquire information from a field situation. Experimental elms were located in the MSU stadium nursery. They represented a perfect field situation for a preliminary investigation. At this point getting approval to do this preliminary experiment became important.

The rationale that I used prior to proceeding with the field experiment was as follows:

1. The transposon generated bacterium used in this study fell "outside" of the NIH guidelines. It was shown by us not to contain any man made DNA ligations. Also to my best knowledge federal agencies dealing with biological systems have consistently followed these guidelines and definitions since they were originally formulated by NIH in 1977-1978.

2. Some elm trees, having been treated via a root injection method with the bacterium, and showing no adverse effects, were planted in the MSU stadium nursery in 1982. I knew of no federal nor MSU Biosafety Committee regulations existing at that time precluding introduction of this bacterium into the field. Thus,

this bacterium already existed in the exact location where it was again to be introduced in the 1987 experiment. Some data exists to show that it was still present in the roots of at least 2 trees in 1987. To me, it seemed illogical that any regulations should apply to a situation in which a prior release had occurred.

3. I had learned that in 1984 the USDA had no regulations controlling the use or release of transposon mutant bacteria used in biocontrol of a plant disease as long as it was in a field less than 10 acres. This information confirmed my earlier assumptions.

4. In late May, 1987, a colleague in my department informed me that I should call the EPA which I did the first week of June. I explained to the official that I planned to field test a transposon mutant of my bacterium. I also explained that I had only a narrow window of time 3-4 weeks of June to do the experiment - otherwise I would have to wait an additional year. He indicated that a review was necessary and that it would take 60-90 days. I incorrectly assumed that once he realized that it was a single transposon mutant of an indigenous bacterial strain he would know that it was not in the EPA purview since they had consistently followed the NIH guidelines. I knew nothing of the June 26, 1986 Fed. Register p23302-23393 statement that "genetic engineering is defined as genetic manipulation of an organism by procedures other than those used in classical genetics..." p 23354. This definition is contradictory to that used by NIH for

the past 10 years and under which I had been doing my experiments.

I reasoned that since there was no apparent NIH infraction, and the USDA had already given an earlier ruling, and since MSU is a land grant institution under the purview of the USDA, I could proceed with eventual assurances that EPA who generally follow the NIH guidelines would have given the experiment their blessing. This was incorrect.

I wrote an application letter to EPA on June 15th and started the field experiment on June 18th. A portion of the experiment would take 90 days, and another would take 2 growing seasons.

The size of the test plot was small, and the bacteria were inside the tree (like a container), since they were injected into the tree with a gouge pistol. Furthermore, the bacterium had been tested in the greenhouse over the course of 2-3 years on seedling elms with no adverse effects.

In early July an official called me from the EPA explaining that they had received my application, and I voluntarily and honestly told him that I had started the field test and that I would be willing to stop it at any time at their request. Two weeks later an investigating team (4 people) arrived in my lab from EPA and questioned me, and examined the elms. To my best knowledge their report will show that 1) some alleged violation of regulatory approval had occurred ; 2) there was no threat to human health and safety, and; 3) all bacterial injected elms had

been protected from the ravages of Dutch elm disease, while the remainder (controls) had died.

I had not contacted the MSU biosafety committee until early July, at least 2 weeks after the experiment had begun. I did so at the request of MSU V. P. Jutila. Prior to the test, I did not deem it necessary to contact the MSU Biosafety Committee since the NIH guidelines were not in effect for the organism that I was testing. A hearing was conducted at MSU on August 28 to learn what violations of federal regulations had occurred. It was fair and professionally conducted. On that same day the EPA issued a reprimand and a few days later so likewise did MSU President William Tietz. It was not until then did I realize what specific EPA regulation had been violated.

I believe in honoring and obeying the law, and I do not challenge the right of the USDA, EPA, NIH, and the local biosafety committee to impose regulations to control the release of potentially hazardous and pathogenic organisms into the environment. This is in the best interest of the public. While I honestly did not believe that the organism in question in this experiment was covered by those regulations, obviously, because of the interest in this topic and the need to control the release of potentially harmful organisms, I should have made better and more frequent contact with all of the regulatory bodies prior to conducting the experiment. While that may not be an excuse for what has happened, it does point out the uncertainty about the application of the regulations because of their size, their

proliferation, their lack of clarity, and their availability.

I have recently learned (October 1, 1987) from an EPA official that had I released the bacterium on June 21, 1987 (Fed. Register), 3 days after I started the experiment, I would have been in violation of the USDA-APHIS regulations - their definition of genetic modification includes, in part, any organism made with recombinant DNA techniques. This definition is definitely different than that of NIH. Even had I received permission from EPA does this mean that I would also need permission from APHIS? If so, it would appear that the regulatory process is more cumbersome than I can possibly imagine.

At the outset of the experiment, one of the reasons for my confusion was that I had received mixed signals from various federal guidelines and officials. The need to get on with the experiment was uppermost in my mind. I expressed to EPA officials a willingness to terminate the experiment at any time during the course of the season. I appreciate the kind and friendly help from EPA personnel throughout the summer. I have learned that they are honestly trying to perform their job, but in my view it is extremely difficult given the incomprehensible regulations that they are required to enforce.

There was nothing particularly unique about my experiment, nor the circumstances surrounding it. Basically, the events of this case could have happened to anyone. I hope that you can appreciate the fact that it happened with a benign system that

had been previously tested. There was an alert, hard working local biosafety committee doing its best to see to it that regulations were being followed. The difficulty occurred as a result of an ambiguity of federal regulations and ambiguity is comparable to having no regulations at all. Thus, the real issue in this case is how the United States regulates biotechnology.

To me it appears that the proliferation of regulations is putting unreasonable restraints on people who are honestly trying to solve major problems facing our society.

Some of the scientific and technological problems that our nation faces are extremely difficult to handle. On top of this we have imposed a sea of regulatory actions by a myriad of federal agencies with conflicting definitions. The entire effect is one that is absolutely impossible for a scientific researcher (especially in a small business or academic institution) to comprehend and to follow on a regular basis. At the same time there is need for a system to assure the public of the safe application of a new and largely misunderstood scientific discipline. As a voice from the wilderness of America, and as one who has suffered the consequences of this complex system I feel that the time has come for sweeping changes in how we think about biotechnology and how we regulate it.

I feel that in order to expedite the development and progress of biotechnology in the United States, at the same time providing safeguards to the public we should consider the following brief recommendations (goals) and methods of

implementing them.

Goal 1) We need to develop a single document - a "constitution of biotechnology" that is readily available to all practitioners, institutions, biosafety committees and companies doing biotechnological activities in the United States. Such a document should be easy to read, rational, and workable.

Implementation: Congress should commission the National Academy of Sciences to prepare such a document with help from the public, the scientific community, and an interagency group of federal personnel. It should be adopted after careful review and wide dissemination and discussion and it should appear in a loose leaf format.

Goal 2) A single lead agency should be identified to be a clearing house for information, for permits, and for general assistance to the scientific community. Furthermore, local biosafety committees need to be involved and have the flexibility to make decisions.

Implementation: No single individual nor scientific establishment identifying a particular problem should be compelled to work with more than 1 federal agency. If a multitude of agencies absolutely need to be involved in regulating biotechnology - they must all work with the same document. Nevertheless, one clearing house agency should be identified for the case at hand. No new bureaucracy should be created and the chaos needs to be eliminated!

Goal 3) We need to more carefully examine the regulations

that are in effect or are being proposed especially in those cases in which we know of little or no risk.

Implementation: In view of the August 1987 National Academy of Sciences report, many biotech activities and many organisms pose no risk nor harm either to man nor the environment. Efforts to solve a myriad of health and environmental problems by subtle biological means, rather than by harsh physical or chemical means should be encouraged. Regulations that are imposed for no apparent reason are a harm to science and the eventual well being of our citizens and their environment. As we learn more, provisions should be made for a rapid change in regulations. To me it appears that burgeoning regulations by a number of federal agencies is reflecting just an opposite position namely we are placing regulations, restrictions, permit requirements on organisms and technologies that are known to be harmless.

Goal 4) We need move away from operating under a position of fear and concentrate on the total economic and beneficial effects of biotechnology while keeping the safety of the public uppermost in our mind.

Implementation: Certain aspects of biotechnology especially in the release of certain organisms need more federal attention, not from the standpoint of regulation, but of support for scientific research to acquire new uses and benefits of this technology. NSF, USDA, EPA and are all in a perfectly good position to become involved in this activity. Such knowledge gaps have been recently identified by OTA. My limited, but

dreadful experience indicates that more effort needs to be made to educate the general public on all aspects of biotechnological sciences. We cannot, however, expect the press, much less the general public, to even begin understanding this field of science if the primary definitions are conflicting.

In the near future, I am hopeful that America will see the tremendous benefits and blessings of research in the field of biotechnology which is currently overregulated. Biotechnology and its subfield of genetic engineering has the potential to solve many problems associated with our growing and complex society including those of human, animal and plant health, environmental problems, and food production. In addition, the future seems bright for this technology to help America solve some of its economic problems and improve its competitive edge. Genetic engineering is not something to be feared by the public, but something to be used to bless our land. Groups of well meaning scientists who hold the public trust are the mainstay of this activity.

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Statement of

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Before the

Senate Committee on Environment and Public Works' Subcommittee
on Hazardous Wastes and Toxic Substances

November 5, 1987

Mr. Chairman, Members of the Subcommittee:

My name is John Jutila. I am Vice President for Research at Montana State University and Professor of Microbiology. My 31 years of professional involvement in basic research, administration, teaching, and public service provide the background for my remarks.

I am very grateful to have this opportunity to testify before the Subcommittee regarding the regulation of biotechnology research.

I do not intend to focus on the specific incident that occurred at Montana State University last summer about which Dr. Strobel has just briefed you, except insofar as the MSU experience can provide constructive guidance in this review. Indeed, I believe we are fortunate to have had this experience. The incident proved to be without serious negative environmental consequence and yet appears to be of sufficient public interest to prompt a review of the policies and procedures involved. Hopefully, the outcome of such a review should be to enhance the performance of a young but enormously promising field of research and ultimately improve the quality of our lives.

Statement of the Problem

The Montana State University experience demonstrates the need for a rationalization and clarification of the federal policies and regulations surrounding biotechnology research in general and those involving recombinant DNA technology in particular. Dr. Gary Strobel is an internationally-known scientist with a distinguished record of research achievement. And yet, even an individual with his experience managed to run afoul of the federal regulatory system.

The incident triggered by Dr. Strobel's experiment and the investigation that followed pointed up a number of problem areas that academically-based scientists encounter with the current welter of rules and regulations pertaining to biotechnology research. These problem areas create confusion for the scientist and the research administrator alike and tend to lead to public controversy as well. The result of such confusion could be the needless inhibition or restriction of valuable research.

The first problem area has to do with the need for clarification and definition of terms. The development of a unified nomenclature would allow the various entities involved to delineate their roles and jurisdictions in the regulatory system. Without such clarification, there can be no rational identification of who the key players are in the development and administration of policies and procedures.

The second problem area lies in the need for the development of coherent coordinated policies and procedures that will regulate, guide and foster the growth of biotechnology research. Hopefully a framework for policy development can be devised that will prove to be flexible and dynamic as the scientific base evolves and grows.

The third problem area then has to do with the organizational restructuring required to administer the policies and procedures developed.

Recommendations

It is fortunate that this hearing is occurring on the heels of the recent publication of the National Academy of Sciences (NAS) entitled "Introduction of Recombinant-DNA-Engineered Organisms into the Environment:

Key Issues." This document represents the collective judgment of the most respected members of the scientific community and therefore our review need not reexamine in great detail the issues already addressed by scholars in this area. Copies of the full report are appended to this testimony although I believe certain pertinent parts bear quoting at some length here.

The report deals specifically with the relevant scientific principles and experiences which should govern the decision to introduce into the environment organisms modified by recombinant DNA (R-DNA) techniques. Based on a scientific assessment of past of experience with the release of genetically altered into the environment, not based on the method of modification of the organism, the committee proposed the formulation of coherent, scientifically-based regulations that stimulate development and uses of such organisms.

The report states, "Mounting concerns about environmental degradation, together with the pressing problems of ensuring adequate food and health care for a rapidly expanding global population, provide a compelling rationale for the accelerated study and development of biological organisms for use in agriculture, health care, and biosphere management."

The findings and conclusions of this report give us guidance with respect to the course of action we must consider for the future.

First, there is a need to aggregate existing guidelines from all agencies and offices having a voice in the regulation of biotechnology research. These existing guidelines need to be assimilated into a coherent and comprehensive listing of definitions of terms and principles to discriminate among organisims and their release that differ in their

potential to cause environmental problems. The identification of resources and their aggregation into a workable format with a common language would greatly facilitate the development of a policy framework that would serve as the basis for universally accepted guidelines. Dr. Strobel has refered to these as a "constitution of biotechnology." A national commission of knowledgeable persons from the academic community, industry and government working in concert with an interagency group should be charged by Congress to develop such a document. It should be designed in such a way as to be responsive to change as new knowledge is developed. Such guidelines may mimic those of the National Institutes of Health and should be reconstructed in accord with the findings and conlusions of the NAS panel.

Second, in response to the universal guidelines, there is need to develop rational policies and procedures for the administration of rules and regulations that emerge from these guidelines. The NAS report addresses this issue with the following conclusion:

> "The timely development and the rational introduction of R-DNA modified organisms into the environment depend on the formulation of sound regulatory policy that stimulates innovation without compromising good environmental management."

The stringency of regulations should be relaxed and amended as the scienctific knowledge increases. For example, in the early 1970's when gene splicing technology was first being employed, it seemed to be such a powerful methodology that many scientists were fearful that the resulting

new life forms posed a serious threat to the environment. The emergence of an "andromeda strain" has not occurred and the fears of the most devoted science fiction advocates regarding a "monster bug" have failed to materialize.

The report of the National Academy of Sciences panel would seem to support this contention. It says in part, "There is no evidence that unique hazards exist either in the use of R-DNA techniques or in the movement of genes between unrelated organisms."

Third, there is need to establish an interagency group that assists each regulatory agency with the task of bringing scientific advances into a management scheme in accordance with unified by the universal guidelines. The scientific community-at-large should provide guidance on a continuing basis in the redefinition of terms and continual reformulation of policies responsible for the regulation and performance of biotechnology research in general. The continuing success of any regulatory system depends on its ability to respond to changing conditions and in the regulation of cutting edge scientific activity, this quality is particularly crucial.

Finally, I wish to comment on an issue of great concern to me, that of local or institutional participation in regulation. We discovered through the MSU experience that the appearance of disagreement among scientists or between scientists and regulators quickly leads to public controversy even though original public interest in the subject matter may have been slight. While people control risk, the public perception is that the risk is greater if those in control are unknown or if controls are imposed from far away. Risks involved with the application of new technologies are perceived to be known and small if they are managed up close, if locals have a voice in the

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approval process. A sense of familiarity and proximity tends to enhance the credibility of scientists and the products of their work.

For this reason, care should be given in the formulation of policies pertaining to the structuring of federal regulatory mechanisms and their implementation at the local level. We found in the MSU experience that the conventional university Institutional Review Board system (IRB) works very well and we recommend that the review, evaluation and policing functions of scientific regulation continue to be delegated to the institutions at which the research is occurring, with federal oversight only of procedures and processes. Those who are vested with the power to regulate must have respect and credibility and this is enchanced by familiarity and proximity. The retention of review processes and the effective management of biotechnology research must be retained at the local level.

Conclusion

There is no question that the caliber of American science would be adversely affected if more restrictive rules and remote mechanisms of enforcement were implemented by the federal agencies. I firmly believe that a review of the current regulations and their administrative context could yield an improved system that would continue to facilitate biotechnology research as new knowledge becomes available. Further, a coherent delineation of federal policies would facilitate the operation of local review processes and better guide our progress. The bottom line, I believe, is an enhanced research environment that helps fulfill the promise of biotechnology research as it pertains to improving human health and environment.

Please accept these comments as constructive recommendations in support of the review process.

Thank you for your attention.

Testimony for Senate Committee Hearing, 5 November 1987

Senator Baucus and members of the Subcommittee on Hazardous Wastes and Toxic Substances, I appreciate the opportunity to testify and offer some of my thoughts and concerns, as a scientist (Dr. Larry W. Moore, Plant Pathologist, Department of Botany and Plant Pathology, Oregon Sate University, Corvallis, OR 97331), on the effectiveness of current Federal regulations of biotechnology.

One of my concerns has to do with the perception of some of our populace that biotechnology holds many dangers. It would seem that some people equate these perceived dangers with maladies such as AIDS. Yet, ultimately, the methods of biotechnology will probably provide the best means of detection and treatment of the virus causing this disease. Our challenge in the face of these perceptions is to maintain a calm and reasoned outlook relative to public safety and at the same time encourage scientific inquiry and application in the biotechnology arena.

It is indeed encouraging that a high percentage of the public supports continued research in biotechnology (1987 Office of Technology Assessment report entitled "New Developments in Biotechnology. 2 Background Paper Public Perceptions of Biotechnology", 1987.). This same report indicated that the public had greater trust in scientists from academic institutions than from any other organization relative to biotechnology issues. To enable maximum scientific progress, it is very important to maintain and foster that trust. With this need in mind, we can only hope that the recent disclosures and notoriety given to Dr. Strobel's experiments will not erode that public trust. Although Dr. Strobel states that he acted in frustration, his actions could precipitate public and legislative repercussions that would impact adversely thousands of other scientists who have been equally frustrated by the same confusing array of regulations (but exercised patience).

The remainder of my testimony is organized around several questions which I see as subsets of the overall issue.

First, is the present regulatory structure, as outlined in various issues of the Federal Register and in particular the 26 June 1986 issue, understandable to most scientists? My answer is no. It takes a great amount of study to understand most of the regulatory materials that have been presented in the Federal Register about biotechnology issues because of the complexity of the language, diversity of definition of terms and procedures from one Federal regulatory agency to another, the long length of these documents, and the relative "obscurity" of the Federal Register to numerous scientists. Another factor which may have contributed significantly to the problem is the enormous number of scientific publications

which scientists should review to stay current with research pertinent to their own field of endeavor. For example, it has been reported that the number of research papers published in agriculture and biology doubles every 2 years; the doubling time is even shorter in the area of biotechnology. In short, complex writing which is difficult to read and understand probably gets superficial attention.

Second, is the present regulatory structure inhibiting unduly research and development in biotechnology? I answer yes but with some equivocation. Part of the restrictive regulation has been triggered by law suits enjoined by advocacy groups who are opposed to the very PROCESS of research in the area of biotechnology, let alone the PRODUCT of the research. Because of this pressure, I think administrators of regulatory agencies have often found themselves in a position of "reacting" to situations rather than "acting". However, in retrospect, perhaps the abnormally long delay of 5 years and enormous cost required to field-test Lindow and Panogopolus' ice-minus strain of Pseudomonas syringae wasn't all bad IF it provides us a base line to compare future request for environmental release of genetically released microorganisms. Because of the innocuous nature of this particular genetically engineered microorganism, I think this case has been one of "overkill" relative to insuring public safety. It would be a travesty if it became a precedent of procedure required for all future, similar releases. In the future, there should be different requirements for different levels of risk, with a concomitant reduction in tests over time as field evidence of containment is demonstrated. (This position was also advocated in the recent National Academy of Science report entitled "Introduction of recombinant DNA--engineered organisms into the environment: key issues") and in the USDA Science and Education Guidelines proposed in the Federal Register of 26 June 1986. The forthcoming report from the Office of Technology Assessment provides examples of low risk and high risk).

If a position of regulation based on relative risk is not adopted, I think the consequence of unduly restrictive regulation will be an abandonment by industry of effort to apply biotechnology to commerce. In my own field of Plant Pathology, another consequence of unduly restrictive regulation will be loss of alternative methods to the use of chemical pesticides. It would be ironic if efforts to develop biological control agents, which are designed to reduce the use of and exposure to chemical pesticides in our rural and urban environments, should be stopped (A case in point being the biological agent tested by Dr. Strobel for control of Dutch Elm Disease).

Third, I've been asked at times whether I think the Federal regulatory structure needs to be changed to a single regulatory agency. AFter some thought, my answer is no. The

reason for that answer is that involvement of several agencies provides a diversity of approach to a diverse biology and a system of checks and balances for the entire biotechnology endeavor. No one individual or agency is all-wise, especially after some years of entrenchment. However, I do FAVOR GOOD COORDINATION among agencies, agreement on definition of terms, and uniformity of action across agencies. Lines of jurisdiction among agencies should be optimized to prevent instances of double jeopardy and to minimize loss of time during the review process.

I reiterate that a major concern of scientists is that intellectual endeavor and discovery not be compromised by excessive regulation. Equally important is our societal responsibility to care for the public interest and to provide a rational scheme for public safety. The pivotal question is how these two concerns can best be met.

I urge consideration of a prototype of regulatory guidelines similar to that of the NIH RAC's Guidelines. This request is recommended for the following reasons:

1) The process of investigative inquiry is encouraged and protected best by submitting proposals to the Institutional Biosafety Committee (IBC) for peer review by ACTIVE scientists who are knowledgeable and up-to-date about scientific methodology and progress. These scientists have a "feeling for the organism" with which they work in much the same manner as Dr. Barbara McClintock did with maize (as portrayed beautifully in her biography entitled "A Feeling for the Organism...", written by Evelyn Fox Keller, Freeman Press, 1983). In short, many of the scientists located in our public and private universities across this nation are experts with regard to the biology of the particular germplasm they investigate. It would be prohibitively expensive to assemble such an array of expertise under one or more regulatory agencies. 2) Public safety is reviewed simultaneously with the research because the composition of the IBC includes members form the community. 3) The IBC review is the most EFFICIENT way to pass judgement on the scientist's proposal. 4) Use of the Guidelines simplifies the organizational structure and eliminates erecting another layer of people in the Regulatory Agencies to perform the reviews. Furthermore, these people take permanent positions, and in a relatively short time their knowledge of the cutting edge of science becomes threatened by obsolescence because of their inactivity in the scientific process. 5) The IBC functioning within the Guidelines provides the greatest opportunity for flexibility and diversity. 6) The Guidelines

should be applied uniformly to academia, government, and industry.

Most of the above reasons are embodied in a concept called the National Biological Impact Assessment Program (NBIAP). NBIAP was conceived by the Biotechnology Committee of the National Association of State Universities and Land Grant Colleges (NASULGC). The NBIAP concept provides a flexible mechanism for safeguarding the welfare of the public through an overall coordination of government agencies, the separation of science and regulation, the continued and enhanced use of the Institutional Biosafety Committees (IBC) at each University, and a mechanism for educating the public. Over the past three years, this committee and invited scientists, attorneys, and regulatory personnel have put in many hours to fine-tune the NBIAP concept. The results from these deliberations have been presented orally and in written form at the last three annual meetings of NASULGC. Senator Baucus, I respectively ask that copies of the 1985 and 1986 NASULGC reports containing details of the NBIAP concept be entered as part of my testimony to the Subcommittee as an aid to its investigation and anticipated forthcoming recommendations/legislation.

EPA should continue to regulate the products of biotechnology when they reach commercial level of development. EPA should not regulate research.

APHIS should continue to provide the service that has historically been their strength, which includes the issuance of permits and the licensing of commercial products. APHIS should not regulate research for the reasons cited above that are best handled by the Guidelines. An issue of conflict of interest has been raised about the same agency doing both research and regulation. However, if the three branches under the USDA's division of Science and Educations retain their mandated responsibilities, there should be a clear distinction of responsibility regarding this issue and no conflict of interest. That is, the responsibility of the Cooperative States Research Service (SCRS) and Agricultural Research Service (ARS) is to conduct research, e.g. in the area of biotechnology; APHIS is to regulate the products of this research; and the remaining branch, the Extension Service, is to pursue its traditional role of educating and informing the pubic about the benefits, risk, and use of biotechnology.

I appreciate this opportunity to testify before this hearing on such an important issue. If I can be of any future help, please call on me.

Testimony before U.S. Senate Committee on

Environment and Public Works

Subcommittee on Toxic Wastes and Hazardous Substances and Federal

Biotechnology Regulation

Dr. James M. Tiedje, Dept. of Crop and Soil Sciences, and Microbiology and Public Health, Michigan State University, E. Lansing, MI 48824

I am Dr. James M. Tiedje, a professor at Michigan State University. I have done research and teaching in the field of microbial ecology for 19 years and served 11 years as an editor of Applied and Environmental Microbiology, a major journal in the world that publishes original research in microbial ecology. I have also served on the National Science Foundation and the United States Department of Agriculture Competitive Grant Review Panels and served one year as program manager for one of the USDA Competitive Grants programs. My experience with the issue of genetically engineered microorganisms comes from research projects in this area and service on several panels and workshops on this topic. I currently serve on the OTA panel on New Developments in Biotechnology, on the EPA Biotechnology Science Advisory Committee (BSAC) and the EPA Scientific Advisory Panel (SAP). I have also served on external review panels for the Scientific review of all but one of the proposed releases of genetically engineered microorganisms submitted to EPA. Thus, I have seen how the current regulatory structure works first hand,

plus I have the scientific expertise to judge the quality of the reviews and submissions and the degree of risk.

I have been asked by your staff to focus on the question of whether the current regulatory mechanism is working, whether it can be improved, and if so how.

I first want to state that I believe there needs to be oversight of the introduction of genetically engineered microorganisms and that the oversight should be organized at the Federal level. The reasons I believe there needs to be oversight are: (1) A likely proliferation of state and local regulations in the absence of federal leadership; this would be very stifling to commercial development of these new technologies and I doubt that these groups would have the expertise to adequately perform a scientific review. (2) A substantial portion of the public views this technology as potentially risky and expects oversight. The OTA commissioned Lou Harris Poll, the experience at the California, Missouri, and Wisconsin proposed test sights, and my experience with the general public all convince me that the public views this technology as sufficiently different to warrant oversight. (3) I view that some desired biotechnological products, especially second generation products and later, will carry legitimate potential for risk and thus independent review is important. (4) While regulation is expensive, review and official approval may be important to stable commercial development because it reduces liability and financial risk and thus fosters investment.

It is also important to point out that the potential risk from engineered microorganisms and viruses is, in my view, significantly different from engineered plants and animals primarily because the plants and animals are much more easily recalled or controlled than are the microscopic organisms which would also be released in much higher numbers. Thus it is justified to consider a different level of oversight for the macroorganisms than for the microorganisms. Assuming federal oversight is affirmed then the question is how might it appropriately be done - - effectively assessing true risk and minimizing the burden to the experimenter and the regulatory agencies. I believe that the current framework as organized under the BSCC and using existing agencies and laws is working but can work even better with further experience and refinement. As evidence, the EPA reviews have already become more focused and efficient as judged by comparing the first ice-minus reviews with the most recent Monsanto Pseudomonas lac ZY review. Also based on experience the EPA has developed a new fast track review for genetically modified but non-recombinant organisms which are also included in their FIFRA oversight. Thus with the expected input of new research data on the subject and experience with reviews and field tests both the researcher and the regulatory agency will be better able to focus their efforts on the more critical issues and reduce the burden to both groups.

Successful features of the current framework.

The most important feature of any technological regulatory process is that it be scientifically credible. My judgment is that the scientific reviews have been thorough, comprehensive, and fair. During the first (Ice-minus) review some trivial and perhaps inappropriate issues were raised but

this was due to inexperience and the fact that everyone wanted to be so careful and thorough on the first review. For the most recent ~~later~~ previous this deficiency has been corrected. Thus at least with EPA, the scientific quality of the reviews has been sound. The check and balance provided between agency scientists and the external peer review panels has no doubt contributed to the scientific credibility.

The second feature that has been successful, is the cooperation among regulatory agencies. This is essential for the coordinated framework to work and is something that could easily go awry. But, cooperation especially among NIH, EPA, USDA and state agencies has been impressive from my perspective and these personnel should be complimented and further encouraged in these efforts.

The third successful feature is that all interested parties have had a chance to be heard in the reviews, and when justified, appropriate attention given to all reasonable points. This includes the commercial interests, the public, environmental groups, local communities and academic scientists. By having an open process focused on the technical issues the scientifically credible position rather than the political position is more likely to influence the final decision.

Features that are not yet optimum.

First, as I have alluded to above, the burden of review has exceeded the risk making the development of these research products too costly both in terms of dollars and the time delay to field testing. But, as I've indicated EPA has already substantially lessened the burden due to the experience gained, and their personnel have made extra efforts to speed the review process. Unfortunately, in a litigious society it can be difficult to defend a less comprehensive, though still sufficient review for a proposal of limited risk, at least until enough data and experience are obtained so that lower risk classes and exemptions can be defined and accepted.

Second, under the current framework the level of review can be quite different for scientists in industry versus those in academia and government. This is not a scientifically tenable situation since there is no reason that risk is correlated with the employment sector. If anything, many industry scientists are likely to be more careful since their procedures are often more standardized.

Third, further clarification and coordination of where regulatory authority begins would be helpful. Particularly for academic researchers who aren't accustomed to extensive regulations, the June 26, 1986 Federal Register is confusing. While I admit that part of the fault is a lack of effort on the part of the academic researcher to study somewhat foreign text, compliance is much easier when specifications are obvious and consistent. I have heard from several researchers however that when they have asked EPA staff for clarification, the staff has been extremely helpful.

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Recommendations.

1. It is essential that continued effort be made to evolve a regulatory system that better matches the extent of test data required with true risk. The system should also have the feature of allowing adjustment of the extent of regulatory requirements as more experience is gained.

One approach that may help is to make more use of the Institutional Biosafety Committees in the EPA regulatory structure. This could have several benefits to the researcher: it could reduce the time required for the review process, and it is a more familiar system to the university researcher since institutional committees are already used for research involving isotopes and human subjects and is specified by NIH RAC for laboratory recombinant DNA research. The Institutional Biosafety Committees would need to have a slightly broader membership than many now have, and include an environmental biologist.

A second approach is to continue efforts to define lower risk and exempt categories. Perhaps scientific societies and/or a workshop could devote efforts toward this goal, and thereby facilitate the agencies efforts.

2. To continue to move efficiently toward a well-documented, sound system of regulation and review, continued effort needs to be made for research that supports answering the regulatory uncertainties, and to answer for what principles risk is real or imagined. Many of the scientific questions raised by the risk issue are the type of questions that have never been asked in experimentation before and thus there is not the basic database to underpin the regulatory position or risk questions. Examples are: (i) how frequent is

gene exchange in nature, among what populations and by what mechanisms; (ii) what is the diversity and stability of plasmids and transposons in natural communities, (iii) on what time scale does natural selection work in nature against the less fit population, are there reliable ways to evaluate selection coefficients, (iv) how transferable are principles of macroecology to microbial ecology, eg. how does redundancy of function quantitatively impact risk evaluation of natural microbial processes. Basic answers to these questions would greatly simplify the risk evaluation process. EPA has initiated a competitive grants program for research to support their regulatory needs and have succeeded in attracting an impressive group of projects and investigators. The National Science Foundation also recognized the deficiency in basic science information in microbial ecology and has advertised for proposals in microbial ecology to help correct this deficiency.

3. Efforts toward communication, clarification and coordination of regulatory positions would foster compliance and would be appreciated by the scientific community.

Testimony Before Senate Environment Committee:

Hearings On Biotechnology Regulation, Nov. 5, 1987

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I wish to thank the Subcommittee for the invitation to testify this morning, and to share with you our experiences bringing products to agriculture which are derived from the "New Biology".

Rohm and Haas Company, for which I manage the biotechnology research program, has provided chemical products for agriculture since the 1920's. For the past six decades we have conducted research aimed at developing ever more effective, safer and more environmentally acceptable products to protect food and fiber crops.

For sixty years that research centered principally on chemistry, for with a few notable exceptions biological methods routinely proved less effective. In the early 1980's, however, advances in the biological sciences promised for the first time to allow truly effective use of biological methods for control of crop pests and diseases. And at that time Rohm and Haas, like many other companies, began to invest in agricultural biotechnology research.

Today I would like to review for you one successful part of that research, the development of crop plants able to resist insect attack without the aid of externally applied insecticides. These recombinant plants were successfully field tested in 1986 and again in 1987. As one of the first three field trials of genetically engineered plants, this experience may be considered a test both of the public's acceptance of such work and of the functioning of the new coordinated Regulatory Framework. Therefore, I will briefly summarize the project, and our experience with the public and regulatory agencies leading up to the initial field trial of these recombinant, insect-resistant plants.

Without going into the technical details, let me simply say that under contract to the Rohm and Haas Company a biotechnology firm in Belgium isolated the gene for a natural, biodegradable and non-toxic insecticide and moved that gene into plants. The resulting plants produce minute quantities of the insecticide in their leaves, effectively killing any caterpillars feeding on theplants. The process is easier to watch than explain. The short videotape which follows is a time sequence showing the protection offered by this technique.

(Show video - 1.5 minutes)

About the time we began to consider field testing, the Federal Policy statements of December 31, 1985 were published in the Federal Register. Since these statements designated the U.S.D.A. as the lead agency, we began informal discussions shortly thereafter. At the same time, we notified EPA

and solicited their input. At this time, formal regulations covering recombinant crops were still being drafted, and the U.S.D.A. welcomed the chance to begin evaluating applications submitted on a voluntary basis. Our submission provided their staff with one more "real life" example against which to evaluate the proposed regulations.

Although final rules would not be enacted by U.S.D.A. until mid-1987, we voluntarily submitted an application to conduct field tests to the Animal and Plant Health Inspection Service in May of 1986. Reivew by U.S.D.A. and EPA staff was coordinated by APHIS, completed in September and the first field trial conducted that Fall. Turn around time for review of this application was only four months.

Successful review by the appropriate regulatory agencies was not, however, deemed sufficient grounds to go forward with the trial. We had witnessed the public concern over testing of "ice minus" bacteria despite the compelling evidence of minimal risk. Therefore, we judged it prudent to embark on a public and government communications program to provide accurate information to all affected parties before beginning any testing.

Several weeks before "approval" was anticipated, we met with interested parties at the Federal, State and local levels. For both proposed test sites (Mississippi and Florida) we briefed staff members of the appropriate senators and representatives in Washington. This was followed by visits to the state capitals to meet with representatives of the governors' offices and Departments of Agriculture and the Environmental Resources. Finally, local boards of supervisors, mayors of local cities and county agricultural extension agents were given the same briefings.

To disseminate information to the general public, seminars were planned in both test site communities. Invitation lists were complied from suggestions by state and local officials and included local farmers, business leaders, and local environmental groups among others. Along with a breakfast briefing, we provided a slide show detailing the project, the planned field work and the Federal review process. Finally press briefings were held following each public meeting.

Reception of this communications program was uniformly positive and frankly, quite gratifying. Response from local media and environmental groups was uniformly supportive.

With the communications program completed, we than proceeded with the actual test. Although positive results were obtained, relatively little data came from that first trial. It had been primarily designed to test our protocols and containment procedures. Results of that trial were then used to modify slightly our original application. An amended request was then filed with APHIS in March of 1987. Review was again completed in under four months and a second trial conducted, this time at a breeding station in North Carolina.

Results ofthe second trial were sufficiently encouraging to justify the additional research investment needed to transfer this technology from the test crop, tobacco, to major commercial crops such as cotton, soy and corn. Rohm and Haas is now investing heavily in this research and expects to bring novel, insect-resistant crop varieties to the U.S. market in the mid-1990's, providing a badly needed additional tool to control destructive insect pests.

I understand this Subcommittee is interested today in answering two questions. First, "How effectively is the new coordinated Regulatory Framework functioning?" and second, "Is the current system dangerously lax, appropriate, or stiflingly onerous?"

As is apparent from the history I just recited, our experience only enables me to address those questions as they pertain to recombinant plants. Other witnesses here today are better able to speak to the fate of microbial products under the current system. It might also appear from my testimony that plants, at least, obtaining approval to conduct field trials is already a simple and uneventful experience.

The first test of any system is, of course, seldom either simple or uneventful. I once heard a professional manager say: "When you see a human operation that always runs smoothly look for the guy who's covering up the mistakes, because.....real boats rock". There has been some "rocking" in our experience with the regulatory agencies. This is a "real boat" and is still on its shakedown cruise.

However, the problems we encountered were not major, as the timeliness and thoroughness of our reviews demonstrated. Moreover, I was personally impressed by the efforts the regulatory staff put forth to resolve the inevitable last-minute issues in a professional and timely manner.

In summary we have found that for plants, obtaining approval to field test is neither a time-consuming nor inordinately expensive undertaking.

The second question, "How appropriate is the current level of regulation?" is more complex. If one accepts (as do the U.S.D.A., the National Academy of Sciences, and I) the premise that any risk resulting from use of an organism depends on the properties of the organism itself, and not the process by which it was bred, then there is little reason to regulate recombinant plants at all. Indeed a compelling argument exists that use of recombinant techniques is intrinsically safer than the unregulated traditional crop breeding, since in the latter case dozens of completely uncharacterized genes can be involved. From a strictly scientific viewpoint then, I must agree that recombinant plants are already overregulated.

But this is not a strictly scientific enterprise. It is clear both from recent surveys and from our experiences with testing of recombinant microbes that the public harbors concerns about new technologies. It is equally clear that this technology cannot move ahead without public acceptance. Therefore, at this early point in the evolution of the technology, it is perhaps as important to assure that regulation is based on good science. It is probably essential that we begin with a cautious approach, even at the risk of some temporary overregulation.

I should point out here that, to date, only the first step of the regulatory system for plants has been tested, that covering initial field trials. For agriculture and the environment to benefit ultimately from the advantages of these innovations, much work remains. The current level of scrutiny each test undergoes may be tolerable now, but as these products move into large scale trials in multiple states at dozens of sites, such restrictions could prove prohibitive. A good start has been made, but for the United States to benefit, the regulatory process cannot be frozen in place. The evolution toward identification and exemption from regulation of very low risk products must continue.

I fully expect that in five years government, industry and academia will have accumulated a sufficient data base to exempt many, if not most, categories of recombinant plants from regulation. The U.S.D.A. has already provided a mechanism to do so. Its formal regulations provide an opportunity for anyone to submit a petition with supporting data to either exempt categories from review or add categories not now recognized as embodying risk but which may later be found to pose problems. This approach, starting from a cautiously stringent base to assuage public fears while guaranteeing the flexibility to decrease or increase regulation as experience dictates, offers a workable, if imperfect, roadmap for the advancement of this promising new technology.

Thank you for your kind attention. I would be happy to answer any questions.

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Testimony
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on
Federal Regulation of Biotechnology

Before the
Subcommittee on Hazardous Wastes and Toxic Substances
of the Senate Environment and Public Works Committee
November 5, 1987

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INTRODUCTION

My name is Rebecca Goldburg. I represent the Environmental Defense Fund, a nonprofit environmental group staffed by scientists, economists, and attorneys. I have a doctorate in ecology and head EDF's Biotechnology Program. I thank the Subcommittee for inviting me to present EDF's views concerning this country's biotechnology regulation.

OVERVIEW

The Coordinated Framework for Biotechnology is a policy statement asserting a number of agencies' regulatory authority over biotechnology. The Coordinated Framework "makes do with what we have;" it applies preexisting statutes to biotechnology, which these statutes were not written to regulate. As a result, the Coordinated Framework is a patchwork (some call it crazy quilt), and it is appropriate to ask whether this regulatory policy is working, how it could be improved, and whether we need new biotechnology legislation.

My testimony focuses on the Coordinated Framework's regulation of releases of genetically engineered organisms, the area of biotechnology regulation of prominent concern to environmentalists. Under the Coordinated Framework, releases are regulated primarily by two agencies, EPA and USDA, using four statutes, the Toxic Substances Control Act (TSCA), the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Plant Quarantine Act (PQA), and the Federal Plant Pest Act (FPPA). The FPPA is essentially an extension of the PQA; USDA uses the two statutes together. Most of my testimony will concentrate on these two agencies and four statutes. USDA also has authority under the Virus, Serum, and Toxin Act, and federal funding agencies have authority over biotechnology research they fund.

I have identified twelve ways in which regulation of releases needs improvement. For each of the twelve I will describe the problem and what can be done to correct it. In some cases agency action can correct the problem. In others, amendments to the Coordinated Framework statutes are necessary. Some flaws, however, can only be corrected through new biotechnology legislation.

Releases are being proposed at an accelerating pace. With this increasing demand on agencies, regulatory problems can only be exacerbated, and the chances of detrimental releases slipping through regulatory cracks can only increase. Improving the Coordinated Framework is an immediate concern.

IMPROVING REGULATION OF RELEASES OF ENGINEERED ORGANISMS

a. Problems Correctable by Agency Action

1) USDA's regulatory regime makes minimal provision for public participation in decisions regarding proposed releases. The public is notified about a proposed release only after an environmental assessment for a release is

prepared under the National Environmental Policy Act (NEPA). Public comment is therefore limited to commenting on environmental assessments after they are prepared, and to scoping meetings for environmental impact statements, on those occasions when such statements are prepared. Otherwise, information is only accessible to the public via Freedom of Information Act (FOIA) requests. Of course, since notification about proposed releases is not provided, knowing when to make a FOIA request is impossible.

Because regulation of releases is new, current decisions are setting precedents, and public interest is keen, USDA should encourage--not discourage--public participation. USDA should provide notification in the Federal Register when releases are proposed, thereby allowing the public the opportunity to obtain, examine, and comment on proposals before USDA makes decisions about them. Such a procedure would not constitute a burden to USDA; Federal Register notices need only be a few lines long, and companies already have to provide "sanitized" versions of their proposals to USDA (i.e. versions with confidential business information omitted).

2) There are two ways in which regulation of genetically engineered organisms can be triggered. One trigger is the process by which the organism is made (e.g. recombinant DNA technology). The other is the nature of the organism that is made: the product.

The concern generated by the release of an organism engineered via modern biotechnology should be a function of what the organisms is, rather than how it was made. This is especially true because modern biotechnology can be used to accomplish genetic modifications that could be performed by traditional means (e.g. selective breeding or chemical mutagenesis), as well as modifications not possible previously. Thus it makes scientific sense to regulate the products of biotechnology, rather than the process by which they are made. Furthermore, because modern techniques allow more precise genetic alterations than traditional techniques, in some instances it may be preferable to engineer an organism via modern rather than traditional techniques. Regulating process, rather than product, has the effect of discouraging the use of new techniques.

Under the PQA and FPPA, only organisms produced with recombinant DNA technology and containing genetic material from USDA's list of "plant pests" are regulated by USDA. Because the bacterium currently used as a vector to transfer recombinant DNA molecules into plants (*Agrobacterium tumefaciens*) is listed as a plant pest, USDA in effect regulates plants made by the process of recombinant DNA technology. A growing number of techniques can, however, be used to insert novel genes into plants; thus, simply regulating plants produced by recombinant DNA techniques is incomplete process-based regulation. But, more importantly, USDA would be better off revamping its regulation to emphasize product.

3) EPA has created levels of review (including no review) for engineered organisms based on the nature of DNA source and recipient organisms; thus EPA

has developed product-based criteria to distinguish organisms meriting regulation. Two of EPA's criteria are, however, scientifically questionable and warrant reexamination.

i) The "intergeneric" criterion

Because EPA believes that they are more likely to have novel characteristics, EPA's regulation focuses on "intergeneric organisms" --engineered organisms containing genetic material from different taxonomic genera. With the exception of pathogens, EPA excludes "intrageneric organisms"--engineered organisms containing genetic material from organisms within the same genus--from in-depth regulatory consideration.

Taxonomists classify organisms into genera on the basis of shared characteristics. Genera typically include organisms thought to be closely related, but they are man-made constructs, not biological realities. Organisms classified within the same genus may differ substantially in some ways. For example, eggplant and deadly nightshade are both members of the genus *Solanum*; housecats and pumas are both members of the genus *Felis*.

EPA justifies the intergeneric criterion by asserting that organisms produced with DNA from different genera are more likely to exhibit novel characteristics than intrageneric organisms; but, EPA should also recognize that intrageneric organisms are of potential concern. It's reasonable to retain the "intergeneric criterion" for regulatory convenience. The criterion should be supplemented, however, by a list of characteristics besides pathogenicity that signal a need for in-depth review of intrageneric organisms. Intrageneric organisms engineered to live under new or broader environmental conditions (e.g. organisms engineered to be salt or heat tolerant), to metabolize new substances, or produce new toxins, merit more than cursory review; such characteristics that have a reasonable probability of substantially changing an organism's role in a natural community or of allowing an organism to live in new places.

ii) The regulatory gene criterion

EPA excludes intergeneric organisms containing only "genetic material from well-characterized, non-coding regulatory regions" (i.e. genes that control the amount of product produced by other genes) from in-depth review. EPA's rationale is that the resulting organisms exhibit "quantitative changes in preexisting traits" rather than new traits. But, changes in genetic regulatory regions can dramatically alter an organism's biology. For example, a regulatory region from a different organism could be used to turn genes "on and off" in response to a new environmental signal (e.g. the presence of a chemical). Or, regulatory regions may be used to change an organism's growth or reproductive rate. Because such changes may profoundly affect the role an organism plays in the natural environment, changes in genetic regulatory regions should not be exempted from "intergeneric" consideration.

USDA similarly omits changes in genetic regulatory regions from regulation, and should revise its regulations in a similar fashion.

4) USDA does not require that basic ecological information about an engineered organism--such as the ability of the organisms to survive or compete for resources--be submitted to the agency when applying for a permit for the organism's release. Under the PQA and FPPA, USDA only requires information about the construction and planned use of an organism.

Concerns about releases of genetically engineered organisms center on the role the organism will play in the environment. Will a pesticidal organism injure nontarget organisms? Will an organism designed to degrade a particular substance also degrade other substances we do not want it to? Understanding how an engineered organism is constructed, although providing relevant information, is not adequate to understand its role in the environment. Ecological information, such as a soil-dwelling microorganism's survival rate in runoff water, or the likelihood that an engineered herbicide-resistant crop plant can hybridize with weeds, is necessary to evaluate the impact of an engineered organism. Sometimes such information will be available from the scientific literature; sometimes it will only be obtainable through greenhouse or laboratory testing.

Under NEPA, USDA must prepare an environmental assessment or environmnetal impact statement for every proposed release of an engineered organism it reviews. In order for these documents to be credible, USDA must require that relevant ecological information be submitted with permit applications.

5) Under the Coordinated Framework, some engineered macroorganisms (plants and animals) are not regulated. EPA only regulates engineered microorganisms. USDA regulates some microorganisms and those macroorganisms that meet its plant pest definition. (USDA could also potentially regulate some engineered plants under the Noxious Weed Act.) Other macroorganisms are not regulated. EPA should assert regulatory authority over unregulated macroorganisms under TSCA.

b. Problems correctable by amendments to Coordinated Framework statutes

6) Non-commercial non-federally funded releases are not regulated by the Coordinated Framework. TSCA's function is to regulate releases not covered by other statutes. But TSCA was written primarily to regulate commercial products; its application to non-commercial releases is not as evident. This is of potential concern because recombinant DNA work is not necessarily expensive to perform. (For example, some high schools now teach students recombinant DNA techniques in biology lab.) TSCA needs to be amended to unambiguously cover all non-federally funded releases not covered by other statutes.

7) Under TSCA, it is burdensome for EPA to allow restricted uses of engineered organisms, such as small scale field tests. TSCA was written to allow chemicals that have passed through the "Premanufacture Notification" (PMN) process to be used anywhere, in any amount, and for any use. Release of an engineered organism passing through the PMN process is similarly unrestricted.

The use of small quantities of chemicals for experimental purposes is not regulated under TSCA. But because organisms, unlike chemicals, can reproduce, small-scale field trials of engineered organisms are regulated under TSCA. This poses special difficulties. Without a field trial, EPA will usually have insufficient data to approve an organism for large scale use. Yet, by approving a field trial under TSCA, EPA effectively approves an organism for unrestricted use. EPA has so far circumvented this problem by writing consent orders for field trials under section 5(e) of TSCA. But preparing large numbers of consent orders may not be practical in the future, when EPA must regulate many releases concurrently. TSCA should be amended so that EPA has an alternative mechanism for approving small scale field trials.

c. Problems only correctable by new biotechnology legislation

8) TSCA's "Premanufacturing Notification" (PMN) process makes the statute undesirable for regulation of releases for two reasons. First, TSCA can only restrict the application of a chemical or engineered organism by implementing certain burdensome procedures (section 5(e) consent orders, as discussed in (7), and "Significant New Use Rules"). Because the effect an engineered organism has on the environment will be a function of the particular environment an organism is released into, where and when an organism is released will in part determine the risk associated with a release. EPA may have no difficulty ascertaining that a particular organism poses no significant risk in a particular application, but find it extraordinarily difficult to make that determination for all possible applications --foreseeable and unforeseeable--of the organism. Thus it would be more appropriate for EPA to regulate all releases under a statute that allows EPA to readily grant permits for particular applications of engineered organisms, than a statute was written to allow unrestricted applications of new chemicals.

Second, The PMN process simply allows EPA an opportunity for review. Unless EPA pursues a release proposed under TSCA, release can occur without any review (or any active decision not to review). This is already a common and troubling phenomenon for chemicals. As proposals to release become more frequent, this may also become frequent for engineered organisms. Again, releases would be better regulated under a permit statute.

9) TSCA provides a thin legal basis for the regulation of engineered organisms. TSCA was written to prevent "unreasonable risk of injury to health or the environment from new chemical substances and mixtures." TSCA's newly found authority to regulate new combinations of genetic material was not

Congress' intention and has yet to be tested in court. TSCA should be replaced by legislation with firmer legal footing.

10) USDA is an inappropriate lead agency to regulate releases of engineered organisms for two reasons. First, USDA's mandate is to "protect and enhance agriculture and forestry in the United States." Like all agencies, USDA is bound by NEPA and must disclose the environmental implications of its decisions. But, USDA has no mandate to protect the environment. Even if USDA wants to protect the environment, it has no legal basis for strong regulation. Second, USDA is in the strange position of promoting the development of agricultural biotechnology, while also regulating its products. As experience with the Atomic Energy Commission painfully demonstrated, such divergent goals can only breed internal conflict.

EPA, with a mandate to protect the environment and no vested interest in the development of biotechnology, is the obvious lead agency to regulate releases of engineered organisms. USDA's agricultural expertise is essential for making many decisions about releasing engineered organisms. But USDA should contribute to, rather than be in charge of, regulating releases.

11) Under the Coordinated Framework, more than one agency may have jurisdiction over a release. Although the Office of Science and Technology Policy has created the Biological Sciences Coordinating Committee to try and readjust and define each agency's regulatory powers, overlaps remain. For example, genetically engineered microorganisms that are plant pests but intended for nonagricultural uses will be regulated by USDA under the FPPA and PQA and EPA under TSCA. Engineered microorganisms that are plant pests and intended for pesticidal use will be regulated by USDA under the FPPA and PQA and EPA under FIFRA. Such duplicative authority, the product of patching together preexisting statutes, is potentially wasteful. Having one agency in charge of regulation would be preferable.

12) The Coordinated Framework is confusing and cumbersome. Some applicants may have difficulty deciding what statute(s) apply to a release they wish to propose. Large chemical companies, with legal staffs already familiar with the pertinant statutes, may have minimal trouble following the regulations. But for a start-up biotechnology company, or academic researcher the assortment of potentially applicable statutes and agencies with jurisdiction must seem daunting.

Conclusions

I have described twelve flaws in the Coordinated Framework and ways to correct them. Some, such as USDA's public participation policy, are potentially easy to correct. Others are not, at least as long as the Coordinated Framework retains its current form. All the flaws are correctable by new biotechnology legislation.

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Given the unsatisfactory patchwork nature of the Coordinated Framework, why is there no new biotechnology legislation before us? First, many individuals have put tremendous effort--some of it very thoughtful and diligent--into crafting the Coordinated Framework from meager starting materials. Replacing the Coordinated Framework would mean that earlier effort is wasted. (But, this argument also implies that if we are going to replace the Coordinated Framework, sooner is better.) The second reason is related to the first; now that it is being implemented, there are vested interests in the Coordinated Framework. But, the third reason is most important: Many people, especially those involved in biotechnology, are afraid of new biotechnology legislation. The mediocre status quo is preferable to the unknown. I find it somewhat ironic that individuals who happily launch themselves into a new technology that may revolutionize many aspects of our private and business lives, are frightened by the prospect of new legislation and willing tolerate second-rate regulation.

We can keep the Coordinated Framework and improve it. But, it will always remain the patchwork of statutes with which we decided to make do. This is not good regulatory policy.

Statement of Testimony
Senate Committee on the Environment and Public Works
Subcommittee on Hazardous Wastes and Toxic Substances

November 5, 1987

David J. Glass, Ph.D.
Director, Patents and Regulatory Affairs
BioTechnica International, Inc.

Thank you, Mr. Chairman. My name is David Glass, and I am Director, Patents and Regulatory Affairs at BioTechnica International, Inc. BioTechnica is a six-year old genetic engineering company located in Cambridge, Massachusetts, now employing about 150 people. The company has commercial operations in the areas of agriculture and dental diagnostics, and an advanced research program in production technologies for industrial applications.

Through its subsidiary, BioTechnica Agriculture, of Overland Park, Kansas, BioTechnica is developing an agricultural business through technology development, internal growth and acquisition. The company is actively engaged in developing seeds and microbial products enhanced by genetic, molecular or physical methods that will generate an improved commercial crop. We are particularly aiming at the four major field crops, corn, soybeans, wheat and alfalfa, with the specific goal of creating varieties that are resistant to diseases or insect pests, and developing new crop varieties and other products that will improve the productivity of these crops. Current research efforts involve the use of genetic engineering technologies to insert beneficial new traits into plants, and to improve the utility of agricultural microorganisms.

BioTechnica Agriculture intends to produce and market these products itself, targeting the 10 state midwestern cornbelt region as its major market. The company has established its first agricultural research station, in Pepin County, Wisconsin, which we expect to be the site of the initial field tests for many of our products. BioTechnica has also begun to put into place the marketing and sales force needed to sell genetically engineered products, through the recently-announced acquisition of the McAllister Seed Company of Mt. Pleasant, Iowa.

The company's first products are expected to be improved microbial seed additives for increased productivity of the legume crops alfalfa and soybeans. A naturally-occurring class of soil bacteria called "rhizobia" are capable of forming small nodules on the roots of legume plants, and converting atmospheric nitrogen to a form of this nutrient which the plant can utilize. This process, known as "nitrogen fixation", is the basis for the centuries-old practice of rotating the planting of non-legume crops such as corn with the planting of legumes, which enhances the amount of biological nitrogen available in the soil to the non-legume, thereby increasing productivity. For the past 90 years, American farmers have been able to buy commercial products containing these natural rhizobia, to supplement the amounts that are naturally present in the soil. It is BioTechnica's goal to develop rhizobia that are more effective at nitrogen fixation, by making specific changes to the genes that control the process, using recombinant DNA techniques.

Last year, BioTechnica's first rhizobia product candidates were developed in our laboratories. Greenhouse experiments with these new strains of rhizobia have shown significant yield increases in alfalfa in the early stages of plant growth. The next step is to test these strains under the more demanding, but more realistic, conditions of the field, to begin to assess their true usefulness to the farmer.

Over the past few years, BioTechnica had been holding informal consultations on the rhizobia project with both the Environmental Protection Agency and the U.S. Department of Agriculture, as both these agencies were developing their regulatory programs for biotechnology. Following the issuance of the final version of the "Coordinated Framework for the Regulation of Biotechnology", in the June 26, 1986 Federal Register, BioTechnica began meeting more formally with these agencies, to discuss how our initial field test would be regulated. These pre-notice meetings focussed on discussions of jurisdiction over the test under the Coordinated Framework, and the data requirements for regulatory review.

The genetically engineered rhizobia seemed clearly within the scope of the regulations under the Plant Pest Act which USDA had proposed in the June 26, 1986 Federal Register (which have since been issued as a final rule). The question remained as to whether the microorganisms would also fall within the scope of EPA regulation. EPA has never regulated rhizobia products as pesticides, and these organisms have no pesticidal activity, so they were clearly outside the scope of the pesticide law, FIFRA. However, as genetically altered microorganisms not subject to regulation under statutes such as FIFRA or the Food, Drug and Cosmetic Act, these organisms were potentially subject to EPA regulation

under the Toxic Substances Control Act, as the agency proposed in the Coordinated Framework. Under the Framework, the organisms would be subject to the premanufacture notification requirements of TSCA if they were "intergeneric"; that is, if they contained genetic information arising from organisms of more than one taxonomic genus. BioTechnica's genetic engineering work involved only the manipulation of genes from within the Rhizobium genus; however, the DNA vector which was utilized as the vehicle to make the desired changes arose from a different genus. On this basis, EPA decided that our organisms were "intergeneric", and therefore subject to premanufacture notification (PMN) under TSCA.

Ordinarily, TSCA includes a research and development exemption for the use of limited quantities of new chemical substances. A research field test of the limited scope which BioTechnica was to propose would ordinarily qualify for this exemption, so that no PMN would be required. However, in the Coordinated Framework, EPA maintained that since a microorganism released into the environment is potentially able to multiply beyond its original numbers, it proposed to remove the R&D exemption for outdoor uses of any microorganism subject to TSCA, and requested voluntary compliance with this policy until the agency could complete the necessary rule-making.

BioTechnica, in voluntary compliance with this policy, submitted three PMNs on February 6, 1987, describing three recombinant strains of Rhizobium meliloti which the company proposed to field test at its Pepin County, Wisconsin field station. These were the first biotechnology PMNs to be submitted to EPA under the policies outlined in the Coordinated Framework. BioTechnica also submitted the same materials to the USDA

Animal and Plant Health Inspection Service (APHIS), for its review under that agency's proposed Plant Pest Act regulations.

The submissions consisted of a document of nearly 100 pages, describing the genetically engineered microorganisms, the design of the proposed field test, and the precautions under which it would be conducted. The proposal also contained a detailed summary of the biology of R. meliloti and its interaction with alfalfa, along with a review of the considerable body of scientific literature concerning the ecology and environmental behavior of naturally-occurring rhizobia. The more important of these scientific papers were included among the 250 pages of attachments submitted with the document. Finally, the company reported the results of greenhouse tests we conducted to assess the potential environmental effects of the specific genetically engineered strains which we were proposing to test in the field.

Both EPA and USDA began independent reviews of the submission, coordinating their efforts as they did so. Later in the process, the corresponding state agencies in Wisconsin (the Department of Natural Resources and the Department of Agriculture, Trade and Consumer Protection) also became involved in the review. Both federal reviews involved qualified scientific experts both within the agencies and without. In EPA's case, the agency convened a special subcommittee of its Biotechnology Science Advisory Committee, which held a public meeting in March to review the proposal. In conjunction with the state agencies, EPA and USDA conducted a site visit to the company's research station. EPA announced the receipt of the PMNs in the Federal Register, made the submitted materials available to the public, and solicited public comment on the proposal.

During the course of the regulatory review, BioTechnica conducted a community relations program in Pepin County and surrounding areas. This program consisted of individual meetings with a variety of community leaders in business, government, and farming, university scientists, environmental groups (at both the national and state levels), and other interested citizens. The company sponsored an open meeting to present our plans and answer questions, conducted tours of the research station, and also appeared at several legislative and regulatory hearings at several locations in Wisconsin. Finally, the company established a citizens advisory committee in Pepin County, which included scientists from the University of Wisconsin, and which held a public meeting to review the plans for the field test. We expect this committee will continue to review other field test proposals in the future. Although some level of concern was naturally voiced by a small number of Pepin County citizens, BioTechnica was able to gain considerable community acceptance and support for the proposed field test.

EPA's scientific review of the proposal was fair and thorough. The agency considered a variety of potential environmental effects grouped into two categories, hazard assessment and exposure assessment, which were then integrated into a risk assessment. Among the possible environmental effects considered were several which were brought to EPA's attention by outside reviewers or by members of the public. In fact, the agency received many helpful comments from members of the public and from environmental groups such as the Environmental Defense Fund and the Conservation Foundation.

EPA concluded its preliminary assessment within the ninety-day review period specified by TSCA, at which time (May 1987) it announced a preliminary approval for the field test, based on its assessment that the test as proposed would not present unreasonable risks to human health or the environment. The company and the agency agreed on a 60-day suspension of the review period to allow more time to accomplish two tasks: the submission and review of additional information on the protocols for conducting and monitoring the field test; and the development of an appropriate consent order under Section 5(e) of TSCA, which would allow BioTechnica to proceed with the proposed small-scale field test without allowing any expanded testing or manufacture of the products.

BioTechnica and EPA made excellent progress on the language of the consent order, and had agreed on nearly-final language by the end of June. In the meantime, the company submitted almost all the information requested by the agency, including a detailed plan to monitor the fate of the microorganisms in the environment, and this information underwent review by EPA and the other agencies.

As these reviews were being finalized, BioTechnica made an unexpected discovery which jeopardized the validity of the proposed monitoring plan. The company intended to track the fate of the organisms in the environment through the use of genetic markers; in this case, genes which confer upon the organism resistance to certain antibiotics which would otherwise be lethal to the organism. This approach could only be valid if the proposed markers were unique; that is, if they were not present in significant number among the billions of naturally-occurring microorganisms in the soil. EPA had requested data from BioTechnica as to the numbers of such antibiotic resistant organisms

in the Pepin County soil. BioTechnica gathered this data in July, and made the unexpected discovery that the natural levels of these antibiotic resistances in the soil were significantly higher than expected, enough so that the original monitoring plan was no longer valid. Since it was not possible to correct the problem in time to conduct the field test this year as planned, BioTechnica asked EPA for a longer suspension to the review period, to allow time for the development of a suitable monitoring plan. BioTechnica submitted a revised monitoring plan earlier this month, based on different resistance genes which we have shown to be capable of distinguishing our strains from the naturally-occurring soil microorganisms. This new plan is now being reviewed by the federal and state agencies, and we expect this review to be complete by the end of the year. The field test is now scheduled for the spring of 1988.

The reviews conducted by USDA and the Wisconsin state agencies followed a similar course. By May or June, each agency came to its own preliminary conclusion that the test posed low risks and should be allowed to proceed once an acceptable monitoring plan is adopted. USDA and the Wisconsin Agriculture Department will be cooperating in the adoption of an environmental assessment and finding of no significant impact, which will accompany the final decision from these agencies.

Although the review process has not been completed, BioTechnica is able to offer its perspectives on the regulatory process as it has been applied to our proposal. The major points can be summarized as follows.

<u>The current regulatory framework works in practice</u>. Our experience clearly shows that the federal government is able to conduct a review of a proposed biotechnology field test under the Coordinated Framework. EPA and USDA were able to work together quite adequately in coordinating

their reviews, and both agencies were able to work with their counterparts at the state level. Since BioTechnica's proposal was one of the first to go through the process, there were guaranteed to be instances where certain procedures were carried out less efficiently or more slowly than desired. EPA has already learned from the BioTechnica experience, as shown by the efficient way in which they were able to review Monsanto's proposed field test of a genetically engineered Pseudomonas, which was scheduled to take place this week. We have no doubts that, as both the agencies and submitters gain more experience with the process, reviews of proposed field tests can be conducted with the timeliness that is required for agricultural projects, without compromising the scienfific validity of the review.

TSCA is adequate for the regulation of biotechnology, and no new laws are needed. The expected products of the new biotechnologies are so diverse as to necessarily require case-by-case regulatory reviews under product-specific laws. BioTechnica's experience under TSCA shows that EPA has the authority to require submission of the data it needs to complete its review, and that the law is flexible enough to allow the agency to conduct reviews that are appropriate.

At this time, the agencies have access to sufficient expertise to conduct reviews, but this may not be the case if the number of applications increases in the future. Both EPA and USDA were able to call upon sufficient expertise from both inside and outside the government to conduct their reviews. However, at EPA in particular, review of the BioTechnica proposal required a considerable allocation of resources, primarily involving in-house staff. It is not clear whether EPA could possibly simultaneously conduct more than one or two reviews of this scope without significantly taxing their already-limited resources.

The last point is of particular importance in light of the incident at Montana State University, which is the subject of today's hearing. Virtually all observers would agree that certain proposed environmental applications of biotechnology present far fewer risks than others. The regulatory process cannot possibly continue devoting such inordinate amounts of time and effort to every field test project that is proposed by industry or academic scientists. While such heightened scrutiny seems appropriate in the early days of the environmental applications of biotechnology, the government must develop a means by which the agencies can devote the bulk of their time to those proposals that are most likely to pose significant risks, while reviewing the less risky proposals in an expedited way.

This point is especially significant because these initial field tests represent an earlier stage of R&D than is ordinarily regulated, and the government must very carefully balance the need to adequately protect the environment against the danger of the unduly hampering innovation by such regulation. For example, the development of improved rhizobia products through classical genetic manipulation has never been regulated at any stage of research or commercial manufacture. BioTechnica, in taking the innovative approach of using the new biotechnologies to improve such products, is being subject to significant regulation as early stages of R&D, which would not be the case for competitors using the classical techniques. Placing innovative companies in such a disadvantage could well deter the development of beneficial new products for American agriculture.

The Montana State incident also points out the difficulties in enforcing regulation of such research activities among the academic community. Companies, even small ones such as BioTechnica, expect a certain amount of government regulation, and assign sufficient staff to monitor and comply with all applicable regulations. Academic researchers are not accustomed to the intrusion of governmental regulation in the research process, and they and their universities are often not prepared to comply with regulations such as these. While no one is condoning the violation of regulations that are already on the books, it is clear that the government must adopt regulatory policies that are enforceable and which will be adhered to by the research community.

EPA has recently made public a proposal that may help alleviate this problem. In a speech to the Industrial Biotechnology Association Annual Meeting on October 22, Dr. John Moore, Assistant Administrator for Pesticides and Toxic Substances, suggested the establishment of "environmental biosafety committees" at institutions proposing to conduct outdoor experiments of genetically engineered organisms. These committees, which would be certified by EPA to include the necessary scientific expertise, would review all biotechnology field tests proposed at the institution, and would have the authority to approve certain classes of experiments deemed the safest, while deferring to EPA on the others.

Although Dr. Moore's suggestion needs to be further developed before the agency is ready to formally propose it, BioTechnica supports this approach as a means of decentralizing the regulatory review process. Inasmuch as the proposal is modelled on the successful use of "institutional biosafety committees" under the NIH Recombinant DNA

Guidelines, there is a high probability that "EBCs" would be accepted by the academic research community as well as by industry, and that they would become an integral part of the regulatory process.

Central to this or any other scheme to make the regulatory process more efficient is the need to distinguish those proposed environmental uses which pose low risks from those that have a realistic potential of having higher risks. In this regard, we endorse the concept that government should regulate the "product, and not the process". As has been noted by many commenters, most recently the report by the National Academy of Sciences entitled "Introduction of DNA-Engineered Organisms into the Environment: Key Issues", there are no environmental risks inherent to recombinant DNA engineered organisms that are different from those associated with non-engineered organisms. Agencies should focus on the potential risks of the product, rather than single out for excessive regulation all organisms produced using a certain technique. In fact, this approach would also lessen the confusion that now exists as a result of the conflicting definitions adopted by the agencies as to what is "genetically engineered". Only in this way can regulatory agencies focus on those proposed applications that truly have the greatest potential for risk.

I hope these comments have been helpful to the subcommitte, and I would be glad to answer any questions at this time.

TESTIMONY OF ANNE K. HOLLANDER,
ASSOCIATE, THE CONSERVATION FOUNDATION

BEFORE THE
SUBCOMMITTEE ON HAZARDOUS WASTES AND TOXIC SUBSTANCES
OF THE
COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS
U.S. SENATE

November 5, 1987

Good morning, and thank you for this opportunity to discuss the effectiveness of the U.S. regulatory structure for products of genetic engineering.

I will provide the Committee with two major observations this morning. First, I am convinced that while the regulatory oversight system is working adequately for the moment, some important improvements are needed. These include:

- Decentralizing some of the environmental reviews, particularly for certain small scale research applications;
- Eliminating regulatory standards that are based solely on recombinant DNA technology;
- Filling the current regulatory gaps for foods and animals;
- Establishing adequate public notification systems at USDA;
- Diverting more funds to ecological research; and
- Planning for long-term staffing needs.

My second major point is that, in addition to undertaking these specific programmatic improvements, I firmly believe the government needs to commission a systematic collection of information on the effects of the biotechnology regulations. This would ensure that in several years, at a hearing like this

one, we will have good, empirical information on the strengths and weaknesses of the policies and their implementation. I will come back to this point later in my testimony.

For the time being, Federal agencies are gaining experience in reviewing products and are conducting reviews at a reasonable rate. In the past year, the Environmental Protection Agency (EPA) and the Department of Agriculture (USDA) have approved several field tests of genetically engineered products under their applicable statutes. More tests have been submitted and are pending approval. Staff at the agencies feel that they are successfully working through the inevitable kinks that occur when building any new program. Industry people with whom I have spoken seem to agree with this, and quite a few say that the federal reviews helped them conduct better risk assessments on their products.

Almost all of the organisms reviewed to date have presented fairly low risks. I expect this will remain true for organisms reviewed over at least the next few years, because the manipulations that researchers are conducting are fairly straightforward and involve organisms that are well understood. Still, considering the fact that the agencies are developing and testing new review procedures and risk assessment techniques for the first time -- and considering that this is the very beginning of a long learning process for the agencies and the industry -- I think these are promising accomplishments.

I do, however, believe some things need to be corrected before much longer. At the moment, I think most of these could be addressed by the agencies themselves; that is, they require policy or procedural adjustments rather than legislative changes. Let me describe some of the improvements I would hope to see in the next year or so.

First, I believe that we need to implement a decentralized approach to reviewing some small scale, research releases. Federal review is costly to taxpayers and burdensome to industry and academia. It also strains the communication resources of federal agencies if they have to ensure that all academic researchers understand the regulations. Federal review should certainly be invoked when necessary, but I believe local level reviews of some lower risk products, perhaps along the lines of the Industrial Biosafety Committee approach used by the National Institutes of Health, can be appropriate, ensure higher compliance, and be much more cost effective.

The agencies that currently rely most on federal review seem to recognize the need to reduce the burden and increase the effectiveness of regulation at the research stage, and they are suggesting that decentralized reviews would be a reasonable step to accomplish these goals. For example, Dr. John Moore of EPA recently indicated that EPA is considering delegating some academic research reviews to local level "Environmental Biosafety Committees" (EBCs). Similarly, the USDA is planning to use its National Biological Impact Assessment Program (NBIAP), which is an existing and very decentralized system, to identify research

sites and to monitor the results of experiments. In the long run, USDA expects the NBIAP system to also conduct risk reviews for environmental releases of organisms.

Such decentralized reviews will have to be implemented very carefully. For example, EPA and USDA will need to ensure that their review boards, however constituted, include members without conflicts of interest, and that the expertness and credibility of their reviews can be demonstrated and maintained. I do not think these are trivial problems, but I do think they can be surmounted.[1]

The decentralized review proposal is an important example of the fact that agencies are aware of some of the problems with the original regulatory policy as described in June, 1986; that they are developing new initiatives that respond to these problems; that these responses can sometimes be accomplished within the existing legislative framework; and that experience with the new policies is an important learning mechanism.

Along with these reassuring signs I see some problems to which the agencies are not yet sufficiently attentive. The next part of my testimony will describe the problems I find most troubling.

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1. The upcoming release of a General Accounting Office report on the Industrial Biosafety Committee system that NIH has established should be very valuable in identifying and addressing potential problem areas.

One issue that concerns me a great deal is that some types of novel products of biotechnology, even though they are clearly on the horizon, are not yet subject to any guidelines at all. Most notable are the lack of review procedures for genetically engineered food plants, and genetically engineered animals -- both domestic animals and wildlife.

I believe that both USDA and the Food and Drug Administration (FDA) have responsibilities for plant foods. Each of these agencies has acknowledged its responsibility for foods in a general way in its policy statements. However, their intentions are not at all clear. They have given no apparent attention to the very important questions of which authorities they will use, what they expect industry to report, how they will review food products, and for what they will review them. For example, will FDA consider all genetically engineered foods to be "generally recognized as safe" (GRAS), and therefore not subject to any reporting requirements? If not, how much change will the Agency allow to be made to a tomato, or a corn plant, before it is no longer GRAS? May it be engineered to express a pest toxin? Will FDA examine the possibility of unintentional nutritional changes?

On the issue of genetically engineered animals I again believe that USDA should have a role, and perhaps the Department of the Interior as well. However, neither agency has examined its authorities or publically clarified whether, or how, it might take on such responsibilities. Certainly USDA has a role as the enforcement agency for the Animal Welfare Act, which ensures

humane treatment of animals. USDA needs to issue guidelines on how that act will be interpreted when applied to genetic engineering of animals. USDA also has a responsibility to inspect animals for human consumption. What about transgenic animals? USDA has acknowledged that the Federal Meat Inspection Act and the Poultry Products Inspection Act might have to be amended to cover such animals (51 FR 23343), but says it will make a decision at such time as they are presented at an official inspection station (this is too late). Also, are food animals subject to FDA's Food, Drug and Cosmetic Act? There are also unresolved questions regarding regulatory oversight of genetically engineered fish or other forms of animals used for food or wildlife purposes. As these organisms are released into the wild, they will present vexing wildlife management and environmental issues.

A second issue that concerns me is the fact that some of the agencies have adopted standards expressed in terms of technology. In particular, the Animal and Plant Health Inspection Service (APHIS) at USDA, and the National Institutes of Health Recombinant DNA Advisory Commitee (NIH RAC), review only organisms derived using recombinant DNA technology for potential health and environmental effects.

While this approach may have appeared reasonable when the RAC was first formed in 1974, I do not think it can be justified any longer, and I was surprised that the USDA took this approach in its regulations issued earlier this year (52 FR 22892). Other forms of genetic engineering that can alter the fundamental

behavior of organisms, such as cell fusion, have been commonplace for several years; new ones such as electroporation and chemical poration are being developed all the time. It is foolish to believe that a standard based on a single technology can be appropriate any longer. Such standards become quickly outdated, and they create regulatory disincentives that discourage the industry from using the regulated technology -- often with effects that are inappropriate or at odds with economic sense or public safety. These problems are inevitable in the current APHIS and RAC approaches.[2]

A third problem needing very much to be corrected is the lack of adequate public notification procedures at USDA. APHIS does not issue any public notice when it receives a request to review a recombinant organism. In marked contrast to EPA and NIH, it also holds no public meetings at which policy and product review issues are discussed. To find out what products are being reviewed by the Agency, interested persons have to submit Freedom of Information Act requests on a routine basis (imagine how little the general public receives, by comparison). I asked USDA whether I could be put on a list to receive notification of new, incoming permit requests, and of approved permits. I was informed that I should send a letter whenever I wanted an update. Responses to such letters can take weeks or months, and

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2. The National Science Foundation (NSF) has the responsibility to review environmental release experiments conducted with NSF funds. It has yet to clarify which types of organisms will be required to undergo this review. If it ultimately adopts a standard based on technology, these same concerns would apply.

would have to be submitted every couple of weeks to keep up with the product flow. This is an unacceptable state of affairs.

One point worth noting is how this contrasts with EPA. Under TSCA, EPA is required to issue Federal Register notices within 5 days of receiving a premanufacture notification. This is not true under FIFRA, but the Agency does it anyway for genetically engineered organisms. Under the Plant Pest Act, USDA is not required to issue special notice either, but it could do so without a legislative change.

A fourth concern I would like to mention relates to the adequacy of the underlying research base on which risk assessments are based. Regulation of biotechnology is placing increasingly large demands on the basic science of ecology -- demands which, in many ways, it is not yet capable of meeting. Qualified scientists have expressed this concern in many forums, so I will not belabor the point here. Instead, I would like to propose a possible approach that would slowly but surely begin to rectify this situation.

Taxpayers have payed hundreds of millions of dollars to develop the scientific knowledge and tools that are now at the foundation of the biotechnology industry. By comparison, they have paid almost nothing to improve our ability to anticipate and control risks from that technology. I believe the time is overdue to change this situation. If we are going to aggressively support the development of a technology, let us also support the scientific knowledge to understand and control it. Specifically, for every dollar of taxpayers' money that is used

to develop biotechnology -- basic and applied research -- some constant percent should be spent on the interdisciplinary research that is necessary to understand its environmental, social, and economic impacts. In that way, as we increase the rate at which the technology develops, we could also commensurately increase our ability to handle it capably.

A fifth problem I would like to mention is the continuing confusion over the role that the USDA Agricultural Research Service (ARS) will play in reviewing USDA-funded research. It has been nearly two years since USDA announced its intention to establish an "Agriculture Biotechnology Research Advisory Committee" (ABRAC) to review environmental release experiments funded by the Agency. We are now told the Committee's first meeting will occur sometime in 1988. ARS also intends to use the National Biological Impact Assessment Program (NBIAP) to identify specific testing sights, and monitor the results of experiments.

While the ARS procedures and committees that are being established may work well once they are in place, the time for action is long overdue. One hears that there are agricultural researchers who have been waiting for years for the procedures, so that they can proceed with their experiments. Even when the committees are in place, at least two major hurdles will be important to overcome. One is the problem of having USDA's ARS, which is clearly an applied research promotion arm of the agency, regulating its own experiments. Establishing a credible review system will be a major challenge for USDA. Second is a problem

that is not unique to ARS but probably will affect it more than any other office or agency with biotechnology responsibilities. That is the problem of overlapping jurisdiction with other agencies. USDA, EPA, NIH and NSF need to resolve the problem of which agency reviews experiments that have multiple funding sources. This problem could become particularly vexing where research is partially supported with federal funds and partially with private, commercial funds, thus putting it squarely in the court of EPA and one of the other agencies at the same time. This seems likely to happen most often with USDA-funded research. I hasten to add that these problems, too, could be resolved without legislative changes if the agencies would give them more attention.

A final problem is that all the agencies need to improve their staff resources to regulate products of biotechnology, but this is difficult for a number of reasons. Good molecular biologists can hold exciting and high-paying jobs outside the government, which reduces the pool of available researchers and product review experts. Also, simply having the budget to expand staffs in a time of tight budgetary constraints is a very real constraint. EPA in particular is going to face this problem because it has a limited number of staff scientists with knowledge of genetics, molecular biology, and ecology. The Agency's historic tendency to focus on human health problems with chemicals will require some significant redirecting in the case of biotechnology, because the potential risks with biotechnology are almost exclusively environmental.

To conclude my comments on the current regulatory scheme, I believe many of the changes that are needed are within the power of the regulatory and research agencies to implement. If they do not, then legislative changes may be appropriate.

This leads to my final point, which I mentioned at the beginning of my testimony.

I believe that Congressional hearings and oversight for the agencies' activities are useful and important; they often provoke the agencies to see and act upon problems that need attention. However, I am also of the opinion that Congress should allow at least two or three more years before making judgments regarding the possible need for new legislation in the area of biotechnology. We simply do not yet have good information on how the reviews are working; most of the information is anecdotal and randomly collected. I have limited my enumeration of problems to those of which I am reasonably confident -- but I would be remiss if I failed to observe that they are almost undoubtedly incomplete. This is true because neither my comments, nor anyone else's at this hearing, are based on the kind of research that would really be desirable before undertaking legislative changes. We are not yet ready to answer the critical questions of whether new legislation is necessary, and if so what form it should take.

For that reason, I am going to conclude with a suggestion. I think Congress should charge the federal agencies with commissioning independent, empirical studies of how their

regulatory procedures are working. These independent studies should examine how the regulations are working -- enumerating substantive and procedural strengths, weaknesses, and costs. They should examine the perspectives of local, state, and federal officials; communities; and industry personnel. Whenever a release takes place, someone should be there to gather this information. People's remembrances are too selective, and sometimes too politically motivated, to be useful after the fact.

Consider this fact: every release experiment has a cadre of natural scientists eagerly regarding these first environmental release experiments as golden opportunities to gather information about the scientific aspects of biotechnology: whether the organisms will exchange genetic material, whether they will be transported beyond the test site, whether they will live or die. These first cases are also a unique and important opportunity for social scientists and policy makers, including Congress, to obtain first-hand information on the effectiveness of the regulatory policies. We should be taking advantage of that opportunity, so that at a hearing like this one, three years from now, there will be good, solid information to report and discuss.